



8EHQ-0304-15427

One Houston Center, Suite 1600
1221 McKinney Street
Houston, Texas 77010
Phone: 713.309.2136
Fax: 713.951.1574
Patrick.gibson@lyondell.com

VIA CERTIFIED MAIL

February 27, 2004

TSCA Document Processing Center (7407M)
Office of Pollution Prevention and Toxics
United States Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, DC 20460-0001

MR 273 672

Attention: TSCA 8(e) Coordinator



RE: 8EHQ Number – 8EHQ-03-15427
Tertiary-Butanol – CASRN 75-65-0
Reproduction/Developmental Toxicity Screening in Rats

Dear Sir or Madam:

In September 2003, Lyondell Chemical Company (Lyondell) submitted information to EPA in accordance with Section 8(e) of the Toxic Substances Control Act and EPA's 1991 Section 8(e) Reporting Guide. In that correspondence, Lyondell reported preliminary information from a reproductive and developmental toxicity screening test (OECD Guideline 421) conducted on tertiary-butanol (CASRN 75-65-0). That submission was assigned 8EHQ Number 8EHQ-03-15427. At that time, the final report for this study was not available. Lyondell has now received the final report and is hereby providing a copy to EPA.

The study was conducted pursuant to the Propylene Carbonate/t-Butyl Alcohol HPV Committee testing plan for the High Production Volume Chemical Challenge Program.

Should you have any questions or require additional details, please do not hesitate to call me at 713-309-2136. I may also be reached by facsimile at 713-951-1574 or by e-mail at patrick.gibson@lyondell.com.

Sincerely,

Patrick Gibson
Product Safety Specialist – Regulatory
Corporate TSCA Coordinator
Lyondell Chemical Company

Enclosure

Cc: TSCA 8(e) Files

RECEIVED
OPPT NOIC
04 MAR -8 AM 10:33



Lyondell Chemical Company

RECEIVED
OPPT NOIC
2004 MAR 15 AM 11:21

CONTAINS NO CBI

CONTAINS NO CBI



STUDY NO. 03-4254

TBA: REPRODUCTION/ DEVELOPMENTAL TOXICITY SCREENING IN RATS

Final Report

Submitted to: Propylene Carbonate/t-Butyl
Alcohol HPV Committee
1250 Connecticut Ave. NW
Suite 700
Washington, DC 20036

Attn: George Cruzan, PhD, DABT
ToxWorks
1153 Roadstown Road
Bridgeton, NJ 08302

Date: 09 February 2004

STATEMENT OF COMPLIANCE

This study was conducted in compliance with EPA Good Laboratory Practices as set forth in 40 CFR Part 792 (TSCA) and the Organization for Economic Cooperation and Development (OECD) Good Laboratory Practices as set forth in ENV/MC/CHEM(98)17.



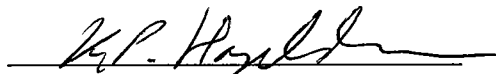
Keith P. Hazelden, BSc., CBiol, MIBiol
Study Director



Date

SIGNATURE PAGE**STUDY DIRECTOR**

The following Scientist was responsible for the overall conduct of this study: (Departmental supervisory personnel are listed on the personnel page of this report, Appendix GG).



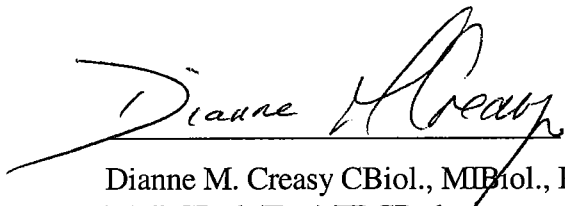
Keith P. Hazelden, BSc, CBiol, MIBiol
Study Director



Date

HISTOPATHOLOGY

The following Pathologist was responsible for the histopathological evaluation:



Dianne M. Creasy CBiol., MIBiol., Ph.D.,
DipRCPath(Tox) FRCPath
Pathologist



Date

SCIENTIFIC REVIEW

The following Scientist has reviewed and approved this report:



Sylvie J. Gosselin, DVM, PhD,
Diplomate ACVP
Senior Vice President, Safety Assessment

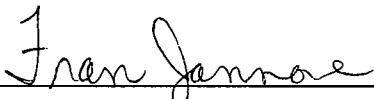


Date

QUALITY ASSURANCE STATEMENT

Listed below are the dates that this study was inspected by the Quality Assurance Unit of Huntingdon Life Sciences, East Millstone, New Jersey, and the dates that findings were reported to the Study Director and Management. This report reflects the raw data as far as can be reasonably established.

Type of Inspection	Date(s) of Inspection	Reported to Study Director and Management
GLP Protocol Review	13 May 03	13 May 03
Dose Administration, Post-Dose Observations & Training Records	17 Jun 03	17 Jun 03
Dose Preparation & Equipment Records	16 Jun 03	27 Jun 03
Dose Confirmation Analysis - Week 1 & Day 8 Stability	17 Jun 03	20 Jun 03
Litter Checks, Training Records & Protocol Amendments Nos. 1 & 2	7 Aug 03	7 Aug 03
F ₀ Terminal Male Necropsy	20 Aug 03	20 Aug 03
Dam and Litter Sacrifice & Protocol Amendment No. 3	28 Aug 03	29 Aug 03
F ₁ Treated Pup Sacrifice – Postnatal Day 28	5 Sep 03	5 Sep 03
Final Report & Study Data	24 & 25 Nov & 1-4, 9 Dec 03	9 Dec 03
Final Analytical Report & Study Data	24 & 25 Nov & 9 & 10 Dec 03	10 Dec 03
F ₁ Treated Animals – Feed Consumption Data and Report Table	06 Jan 04	06 Jan 04
Historical Control Data – Sperm Motility	2 Feb 04	2 Feb 04



Fran Jannone B.A., RQAP-GLP
Quality Assurance Senior Auditor

9 Feb 04
Date

SUMMARY

This study was designed to provide limited information on possible effects of tertiary butanol (TBA), a chemical intermediate, on reproduction and development in rats. Information was also obtained on tolerance to short-term direct exposure (dosing) by offspring immediately after weaning.

Groups of 12 male and 12 female Sprague-Dawley rats received TBA once daily by oral gavage at dose levels of 64, 160, 400, or 1000 mg/kg/day. A Control group of 12 males and 12 females received the dosing vehicle (distilled/de-ionized water) only. The dose volume was 5 mL/kg body weight. Males were dosed from 4 weeks prior to mating until termination after approximately 9 weeks of overall treatment. Females were dosed from 4 weeks prior to mating until termination on postnatal day (PND) 21. Selected weanlings (1/sex/litter) were dosed once daily on PND 21-27 at the same dose levels received by their parents, then terminated on PND 28.

The following parameters were evaluated: For F_0 animals: viability, clinical signs of toxicity, body weights, feed consumption, mating performance and fertility, evaluation of gestation, parturition and lactation, necropsy, sperm analysis, organ weights and histopathological evaluations. For F_1 offspring: survival, clinical signs of toxicity, body weights and necropsy.

Among F_0 animals at 1000 mg/kg/day there was mild to moderate toxicity, including some transient lethargy, ataxia and an initial reduction in male (only) body weight gain that remained as a 5-7% deficit in weight until termination. There was no effect on mating performance or fertility for either sex. During late gestation, the dams showed slightly reduced weight gain, probably as a result of reduced fetal growth *in utero*, then there was significant peri-natal mortality among the offspring: an increased number of stillborn pups and increased mortality up to PND 4 (80% survival of live pups to PND 4), resulting overall in a 30% reduction in pre-culling litter size. Pup body weight at birth was reduced by 10%, progressing to a 15% deficiency by PND 7. In the last week of lactation, this weight deficit was only partially recovered and it remained after weaning (7-12% deficit as compared with Control). During lactation the F_0 dams showed reduced feed consumption, but then in late lactation they showed weight gain instead of the more usual slight weight loss, a pattern of effects that suggested deficient lactation. Increased F_0 male kidney and liver weight at this dosage was suggestive of metabolic induction/accommodation, while a small (8%) increase in testis weight was considered to be of doubtful importance, particularly in the absence of any histological change.

At 400 mg/kg/day there was a lower incidence of transient mild lethargy/ataxia, in females only, beginning after approximately 2 weeks of treatment, but not seen after about the fourth week of treatment. There was no other definite effect at this dosage, in

terms of either reproductive toxicity or more general toxicity, with only a minor increase in male kidney weight, again suggestive of some metabolic accommodation.

At 160 and 64 mg/kg/day there was only a minor increase in F₀ male kidney weight, again suggestive of some metabolic accommodation.

It was concluded that daily treatment by gavage with TBA at 1000 mg/kg/day resulted in mild to moderate toxicity, and although there was no effect on mating performance or fertility, there was significant peri-natal mortality among the offspring. Offspring body weight performance was then deficient.

At 400 mg/kg/day, there was a lower incidence of transient mild toxicity in females only, commencing after approximately 2 weeks of treatment and becoming indiscernible after the 4th week of treatment. This dosage was considered to be a no-adverse-effect level (NOAEL) for reproductive/developmental toxicity.

It was considered that TBA at 160 mg/kg/day represented an overall NOAEL for this study.

There was no definite effect of direct dosing of offspring for one week after weaning at the same dose levels as were received by their parents.

TABLE OF CONTENTS

COVER PAGE.....	1
STATEMENT OF COMPLIANCE.....	2
SIGNATURE PAGE.....	3
QUALITY ASSURANCE STATEMENT	4
SUMMARY.....	5
TABLE OF CONTENTS.....	7
1. INTRODUCTION	11
2. MATERIALS AND METHODS	
2.1. Study Management	11
2.2. Study Dates	12
2.3. Experimental Design.....	13
2.4. Justifications	13
2.5. Test Article.....	15
2.6. Control Article (Vehicle)	17
2.7. Test Animals	17
2.8. Selection/Group Assignment	17
2.9. Animal Identification	18
2.10. Veterinary Care	18
2.11. Husbandry	18
2.12. Mating Procedure.....	20
2.13. Route, Frequency and Duration of Administration.....	21
2.14. Test Article Preparation	21
2.15. Analysis of Dosing Formulations	21
2.16. Test Article Administration	22
2.17. Experimental Evaluations	23
2.18. F ₁ Pup Evaluations	25
2.19. Selection of F ₁ Animals at Weaning	25
2.20. Terminal Evaluations.....	26
2.21. Statistical Evaluations.....	29
2.22. Data Storage.....	30
2.23. Regulatory References	30
2.24. Protocol	31
2.25. Protocol Deviations.....	31
3. RESULTS	
3.1. Dose Formulation Analysis.....	33
3.2. F ₀ Mortality	33
3.3. F ₀ Clinical Observations.....	33
3.4. F ₀ Body Weight Performance	34

3.5.	F ₀ Feed Consumption	35
3.6.	F ₀ Mating Performance, Pregnancy Rate, Duration of Gestation and Gestation Index	35
3.7.	F ₁ Litter Size, Pup Survival and Sex Ratio	35
3.8.	F ₁ Clinical Observations: Lactation Period	36
3.9.	F ₁ Body Weights: Lactation Period	36
3.10.	F ₁ Directly Treated Animals: Clinical Observations and Mortality	36
3.11.	F ₁ Directly Treated Animals: Body Weight Development	37
3.12.	F ₁ Directly Treated Animals: Feed Consumption	37
3.13.	F ₀ Necropsy Findings	37
3.14.	F ₀ Organ Weights	38
3.15.	F ₀ Histopathology	38
3.16.	Seminology	38
3.17.	F ₁ Necropsy Findings	39
4.	DISCUSSION	39
5.	CONCLUSIONS	40
CALCULATIONS		41
REFERENCES		43
GENERAL PREFACE		44
TABLES		
1.	Summary of Survival and Pregnancy – F ₀ Generation	45
2.	Summary of Weekly Clinical Observations - F ₀ Generation	46
3.	Summary of Clinical Observations During Gestation – F ₀ Generation	53
4.	Summary of Maternal Clinical Observations During Lactation – F ₀ Generation	54
5.	Mean Body Weight Values (grams) – F ₀ Generation	55
6.	Mean Body Weight Gain (grams) – F ₀ Generation	58
7.	Summary of Gestation Body Weights – F ₀ Generation	61
8.	Summary of Gestation Body Weight Gain – F ₀ Generation	62
9.	Summary of Maternal Lactation Body Weights – F ₀ Generation	63
10.	Summary of Maternal Lactation Body Weight Gain – F ₀ Generation	64
11.	Mean Feed Consumption (grams/animal/day) – F ₀ Generation	65
12.	Summary of Gestation Feed Consumption (grams/animal/day) – F ₀ Generation	67
13.	Summary of Lactation Feed Consumption (grams/animal/day) - F ₀ Generation	68
14.	Summary of Cohabitation Data - F ₀ Generation	69
15.	Summary of Delivery and Litter Data - F ₀ Generation	70
16.	Summary of Pup Clinical Observations During Lactation - F ₁ Generation	74
17.	Summary of Mean Pup Body Weights - F ₁ Generation	75
18.	Summary of Clinical Observations – F ₁ Treated Animals	79
19.	Mean Body Weight Values (grams) – F ₁ Treated Animals	82
20.	Mean Body Weight Gain (grams) – F ₁ Treated Animals	83

21.	Mean Feed Consumption Values (grams/day)) – F ₁ Treated Animals	85
22.	Incidence Summary Report for Gross Necropsy Observations – F ₀ Generation.....	86
23.	Summary of Parental Organ Weights – F ₀ Generation.....	88
24.	Lesion Incidence Summary with Expanded Severity Levels – F ₀ Generation	93
25.	Summary of Pup Necropsy Observations – F ₁ Generation.....	95
26.	Summary of Parental Necropsy Observations – F ₁ Treated Animals	100

APPENDICES

A.	Analytical Report	102
B.	Individual Animal Termination History – F ₀ Generation	116
C.	Individual Weekly Clinical Observations – F ₀ Generation	126
D.	Individual Daily and Post-Dose Observations – F ₀ Generation.....	142
E.	Individual Clinical Observations During Gestation – F ₀ Generation	153
F.	Individual Maternal Clinical Observations During Lactation – F ₀ Generation.....	158
G.	Individual Body Weights (grams) – F ₀ Generation.....	168
H.	Individual Body Weight Gain (grams)– F ₀ Generation	178
I.	Individual Gestation Body Weights – F ₀ Generation.....	188
J.	Individual Gestation Body Weight Gain – F ₀ Generation	193
K.	Individual Maternal Lactation Body Weights – F ₀ Generation	198
L.	Individual Maternal Lactation Body Weight Gain – F ₀ Generation	203
M.	Individual Feed Consumption (grams/animal/day) – F ₀ Generation	208
N.	Individual Gestation Feed Consumption (grams/animal/day) – F ₀ Generation	218
O.	Individual Maternal Lactation Feed Consumption (grams/animal/day) – F ₀ Generation	223
P.	Individual Mating/Estrous Cycle Data – F ₀ Generation	228
Q.	Individual Mating Assignments – F ₀ Generation.....	233
R.	Individual Delivery and Litter Data - F ₀ Generation.....	238
S.	Individual Pup Sex and Status During Lactation - F ₁ Generation	244
T.	Individual Pup Clinical Observations During Lactation - F ₁ Generation.....	249
U.	Individual Pup Body Weights - F ₁ Generation.....	278
V.	Individual Animal Termination History – F ₁ Treated Animals	303
W.	Individual Clinical Observations – F ₁ Treated Animals	313
X.	Individual Body Weights (grams) – F ₁ Treated Animals.....	331
Y.	Individual Body Weight Gain (grams) – F ₁ Treated Animals.....	341
Z.	Individual Feed Consumption Values (grams/day) – F ₁ Generation	351
AA.	Organ and Final Body Weights – F ₀ Generation	357
BB.	Individual Animal Gross and Microscopic Observations– F ₀ Generation	372
CC.	Individual Pup Necropsy Observations – F ₁ Generation	493
DD.	Individual Necropsy Observations – F ₁ Treated Animals.....	519
EE.	Sperm Analysis Report (Pathology Associates International)	529
	(b) Huntingdon Life Sciences Historical Control Data for Sperm Motility.....	542
FF.	Certificates of Analysis for the Test Article	543

GG. Testing Facility Personnel	545
HH. Protocol and Protocol Amendments	546
II. Report Amendments	581

1. INTRODUCTION

Tertiary butanol (t-butyl alcohol, TBA) is a chemical intermediate used in the production of cosmetics, perfumes, a gasoline additive and components of automobile tires. Under legislation covering the regulation of high-production volume (HPV) chemicals, the US EPA has requested that a reproduction/developmental toxicity screening test (OECD guideline 421) is conducted for TBA.

This study design is intended to provide limited information on possible effects on reproduction and development in rats, in particular on gonadal function, mating behavior, conception, development of the conceptus, parturition, pup survival and growth to weaning. In the present study, the tolerance to short-term direct exposure (dosing) by offspring immediately after weaning was also investigated.

2. MATERIALS AND METHODS

2.1. STUDY MANAGEMENT

2.1.1. SPONSOR

Propylene Carbonate/t-Butyl
Alcohol HPV Committee
1250 Connecticut Ave. NW
Suite 700
Washington, DC 20036

2.1.2. SPONSOR REPRESENTATIVE

Robert J. Fensterheim

2.1.3. STUDY MONITOR

George Cruzan, PhD, DABT
ToxWorks
1153 Roadstown Road
Bridgeton, NJ 08302

2.1.4. TESTING FACILITY

Huntingdon Life Sciences
P.O. Box 2360
Mettlers Road
East Millstone, New Jersey 08875-2360

2.1.5. STUDY DIRECTOR

Keith P. Hazelden BSc, CBiol, MBiol

2.2. STUDY DATES**2.2.1. STUDY INITIATION**

23 May 03 (Date Study Director signed the Protocol)

2.2.2. DATE OF ANIMAL RECEIPT

03 June 2003

2.2.3. EXPERIMENTAL START DATE

03 June 2003

2.2.4. DOSING INITIATION

17 June 2003 - F₀ Animals

27 August 2003 – Directly Treated F₁ pups

2.2.5. DOSING TERMINATION

19 August 2003 - F₀ Males

04 September – F₀ Females

11 September 2003 – Directly Treated F₁ pups

2.2.6. TERMINAL SACRIFICE

20 August 2003 - F₀ Males

11 August to 07 September – F₀ Dams and excess F₁ pups

03 to 12 September 2003 – Directly Treated F₁ pups

2.2.7. EXPERIMENTAL COMPLETION DATE

05 February 2004 (Date Final Report signed by the Pathologist)

2.2.8. STUDY COMPLETION DATE

09 February 2004 (Date Final Report is signed by the Study Director)

2.3. EXPERIMENTAL DESIGN

Group	Group Designation	Dose Levels (mg/kg/day)	Concentration (mg/ml)	Number of F ₀ Animals		Number of F ₁ Animals	
				Males	Females	Males	Females
1	Control	0	0	12	12	12	12
2	Low	64	12.8	12	12	12	12
3	Lower Mid	160	32	12	12	12	12
4	Upper Mid	400	80	12	12	12	12
5	High	1000	200	12	12	12	12

Dose volume: 5 ml/kg body weight, in distilled/deionized water as vehicle.

F₀ males were dosed once daily, seven days/week for 4 weeks prior to first pairing for mating. Dosing continued during the mating and post-mating periods until sacrifice for necropsy and histopathology after an overall 9 weeks of treatment.

F₀ females were dosed once daily, seven days/week for 4 weeks prior to first pairing for mating. Dosing continued during mating, gestation and lactation until sacrifice for necropsy on post-natal day (PND) 21. Females with/without detected evidence of mating, and/or that did not produce a litter, continued treatment for up to 24 days following completion of the mating period, prior to sacrifice and necropsy. F₁ offspring were not treated directly prior to weaning, and those not selected for post-weaning treatment were sacrificed for necropsy on PND 21 or soon after.

F₁ weanlings, 1 male and 1 female from each available litter, were dosed once daily on PND 21-27, at the same dosages applied to the F₀ parents, then sacrificed for necropsy on PND 28.

2.4. JUSTIFICATIONS

2.4.1. ROUTE, FREQUENCY AND DURATION OF ADMINISTRATION

Oral ingestion is a possible route of human exposure to this test article, and once daily dosing by gavage was intended to achieve an adequate regime of continuous systemic exposure. Males were treated for at least 9 weeks overall, to ensure exposure of the

entire process of spermatogenesis. A pre-mating treatment period of 4 weeks followed by a mating trial and detailed histopathological examination of the testes and epididymides was considered sufficient to enable detection of the majority of effects on spermatogenesis and male fertility. Females were treated for the same 4-week pre-mating period as the males, which permitted direct comparison of the gross clinical aspects of any toxicity over that period. Treatment of females continued through to termination at weaning of their litters at post-natal day (PND) 21. This ensured exposure of the female reproductive process from ovulation through conception, implantation, gestation, parturition and lactation. Selected offspring were treated directly for one week after weaning, in order to establish whether or not weanlings would adequately tolerate the dose levels being applied to the adults in the study.

No adverse effects on the sex organs of rats or mice were seen in the subchronic or chronic toxicity studies on t-butanol (TBA) conducted under the National Toxicology Program. In developmental toxicity studies, however, reduced fetal body weight and altered post-natal development were suggested. No studies of the effects of TBA on general reproduction had been conducted and therefore, the present screening study was undertaken.

2.4.2. DOSE LEVEL SELECTION

Previous studies performed under the National Toxicology Program included a 13-week toxicity study in rats and a 2-year study in rats, both by administration in the drinking water at levels of 2.5 to 40 mg/mL (13-week study) and 1.25 to 10 mg/mL (2-year study). The 40 mg/mL dosage proved lethal in the majority of animals in the 13-week study and final body weight of males at 10 and 20 mg/mL was 12% and 17% less than Control. Liver and kidney weights, and the incidence of mineralization in the kidney, were increased at all dosages and there was increased incidence/severity of nephropathy. There was also increased activity of sorbitol dehydrogenase and alanine aminotransferase, with decreased urine volume and increased urine specific gravity. Hyperplasia and inflammation of the urinary bladder epithelium was observed only at dosages in excess of 10 mg/mL.

The 10 mg/mL dosage in drinking water that was applied in the above 13-week study equated to approximately 750 mg/kg/day received dose. Based on the results of that study, the upper dosage in the present study, 1000 mg/kg/day, was expected to cause some toxicity in the F₀ animals, in terms of effects on body weight, liver and kidney weight, and more particularly in males possibly the exacerbation of chronic progressive nephropathy. The 400 mg/kg/day dosage was expected to cause some lesser/marginal toxicity, while the lower dosages were expected to be without discernible toxicity.

2.4.3. TEST ANIMAL SELECTION

The rat is a rodent animal model acceptable under OECD testing guidelines for reproductive toxicity studies. In addition, historical data are available in the Testing Facility with this strain of rat.

2.4.4. NUMBER OF ANIMALS

The number of animals in this study was considered the minimum necessary to allow for meaningful interpretation of the data, as required by OECD guidelines. Ten pregnancies per group are considered adequate numbers for screening for developmental toxicities. The group size of 12 used in this study, with recent pregnancy rates of 80-90%, was intended to provide the necessary numbers for evaluation.

2.5. TEST ARTICLE

Tertiary butanol (t-butyl alcohol, TBA)

2.5.1. TEST ARTICLE CATEGORY

Chemical intermediate

2.5.2. SUPPLIER

Haltermann Ltd.
16717 Jacintoport Blvd.
Houston, TX 77015

2.5.3. LOT NUMBER

HL30408005

2.5.4. PURITY

99.6%

2.5.5. DESCRIPTION

Waxy solid at room temperature. Forms a clear, colorless solution in water.

2.5.6. DATE RECEIVED

08 April 2003

2.5.7. STABILITY, EXPIRATION DATE

No certification of stability is available. A nominal expiry date of 1 year following packaging was allocated by the Sponsors (*ie* to April 2004).

2.5.8. STORAGE

Room temperature, for both the stock test article and the dosing formulations.

2.5.9. ANALYSIS

Documentation of the identity, purity, composition, or other characteristics that define the test article, and the maintenance of these records, was the responsibility of the Sponsor. A Certificate of Analysis is reproduced in Appendix FF.

2.5.10. ARCHIVAL SAMPLE

A sample of the test article is stored in the Archives of the Testing Facility under the conditions specified for storage of this test article.

2.5.11. DISPOSITION

Any unused dosing formulations were discarded daily after completion of animal dosing. Remaining test article will be returned to the Sponsor following completion of the study.

2.6. CONTROL ARTICLE (VEHICLE)

The dosing vehicle was purified (de-ionized) water prepared from tap water supplied by Elizabethtown Water Company (Westfield, New Jersey), distilled at the Testing Facility and stored at room temperature.

2.7. TEST ANIMALS**2.7.1. SPECIES**

Albino rats, Sprague Dawley derived strain (outbred),
CrI:CD (SD) IGS BR

2.7.2. SUPPLIER

Charles River Laboratories
Kingston, NY 12484

2.7.3. NUMBER OF ANIMALS

63 males and 63 females were received, of which 60 males and 60 females were placed on test. The males were derived from a separate breeding room from the females, thus ensuring that there would be no sibling matings in the study.

2.7.4. AGE AND WEIGHT

The animals were approximately 6 weeks of age at receipt and approximately 8 weeks at initiation of treatment, at which time they weighed 248-300 g for males, 165-235 g for females. Females were nulliparous and non-pregnant.

2.7.5. ACCLIMATION PERIOD

Animals were acclimated for 14 days from time of receipt until initiation of treatment. All animals were checked for viability twice daily. Prior to assignment to the study groups, all animals were examined to confirm suitability for the study.

2.8. SELECTION/GROUP ASSIGNMENT

More animals than required for the study were purchased and acclimated. Animals considered suitable for the study on the basis of body weight data and any other pre-test evaluations, were randomly assigned to control or treated groups in an attempt to equalize mean group body weights to

within the range $\pm 20\%$ of the mean weight for each sex. The disposition of all animals not utilized in the study is recorded in the study file.

2.9. ANIMAL IDENTIFICATION

Each animal was assigned a temporary identification number upon receipt. After selection for study, each animal was ear-tagged with a number assigned by the Testing Facility. This number plus the study number comprised the unique animal number for each animal. If the tag was lost, it was replaced. Each cage was provided with a cage card that was colour-coded for dose level identification and contained the study number and animal number.

2.10. VETERINARY CARE

Animals were monitored by the technical staff for any conditions requiring possible veterinary care.

2.11. HUSBANDRY

2.11.1. FACILITIES MANAGEMENT/ANIMAL HUSBANDRY

Currently acceptable practices of good animal husbandry were followed, *eg* Guide for the Care and Use of Laboratory Animals, National Academy Press, 1996. Huntingdon Life Sciences, East Millstone, New Jersey is fully accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC).

2.11.2. HOUSING

F₀ animals were housed individually in stainless steel suspended cages with wire mesh floors and fronts, except for the mating period, when one male and one female rat were housed together. During cohabitation (in the males' cages), the animals were housed in stainless steel cages of an appropriate size. From gestation day (GD) 18 and during lactation, each dam was housed with its litter in a plastic "shoebox" cage with bedding. Each cage was supplied with a glass feeder jar with a stainless steel lid.

F₁ weanlings retained after PND 21 were housed initially in pairs (males and females separate), then individually after PND 22 (as for F₀ animals).

2.11.3. FEED

Certified Rodent Diet No. 5002 (meal) supplied by PMI Nutrition International (St. Louis, MO), was provided *ad libitum* in a glass feeder jar with a stainless steel lid, secured in each cage. Clean jars of fresh feed were provided at least weekly.

Clean feed jars and fresh feed were provided at least weekly for periods when feed consumption was not being recorded and at each interval when feed consumption was recorded.

2.11.4. FEED ANALYSIS

Analytical certification of each batch of feed is maintained on file by the manufacturer. There were no known contaminants in the feed that were expected to interfere with the objectives of this study.

2.11.5. WATER

Water (Elizabethtown Water Company, Westfield, New Jersey) was available without restriction to individual animal cages through an automated watering system.

2.11.6. WATER ANALYSIS

Water analyses are conducted monthly by Elizabethtown Water Company, Westfield, New Jersey (Raritan-East Millstone Plant) to ensure that water meets standards specified under the EPA Federal Safe Drinking Water Act Regulations (40 CFR Part 141). In addition, water samples are collected biannually from representative rooms in the Testing Facility; chemical and microbiological water analyses are conducted on these samples by a subcontract laboratory. Results of all water analyses are maintained on file at the Testing Facility. There were no known contaminants in the water that were expected to interfere with the results of this study.

2.11.7. BEDDING

Ground corncob bedding (Bed-O'-Cobs 1/4 inch Irradiated, The Andersons, Maumee, Ohio) was provided for each mated female rat on GD 18. Fresh bedding was provided every 10 to 11 days, or as needed throughout lactation. There were no known

contaminants in the bedding that were expected to interfere with the results of this study.

2.11.8. ENVIRONMENTAL CONDITIONS

Light/Dark Cycle

A twelve-hour light/dark cycle controlled by an automatic timer was provided.

Temperature

Temperature was monitored in accordance with Testing Facility SOPs and was maintained within the specified range:

Desired Range:	18 to 26°C
Actual Range:	19 to 24°C
Daily Average Range:	19 to 23°C

Relative Humidity

Relative humidity was monitored in accordance with Testing Facility SOPs and maintained within the specified range to the maximum extent possible. Excursions outside the specified range were considered not to have affected the integrity of the study.

Desired Range:	30 to 70%
Actual Range:	44 to 81%
Daily Average Range:	50 to 66%

2.12. MATING PROCEDURE

Within each treatment group the animals were paired, 1 male to 1 female in the male's cage, until evidence of mating was seen or for 2 consecutive weeks. There were no sibling pairings. The females were observed early each morning for the presence of a vaginal plug or of sperm in a vaginal smear. The day on which positive evidence of mating was observed was defined as gestation day (GD) 0. Once mated, the female was removed from the mating cage and housed individually for the remainder of the study. After the mating period was over, females without evidence of

copulation were also returned to individual housing and monitored for visible signs of pregnancy.

2.13. ROUTE, FREQUENCY AND DURATION OF ADMINISTRATION

F₀ males were dosed once daily via oral gavage, seven days/week for 4 weeks prior to mating initiation, continuing through the mating and post-mating periods until termination after a minimum of 9 weeks of treatment. F₀ females were dosed once daily, seven days/week, for 4 weeks prior to mating initiation, continuing through mating, gestation and lactation until post-natal day (PND) 20. Females that did not produce a litter continued to be treated for up to 24 days following completion of the mating period, and were terminated on the 25th or 26th day after the last exposure to a male.

Selected F₁ offspring, following weaning, were dosed once daily on PND 21-27, with termination on PND 28.

2.14. TEST ARTICLE PREPARATION

Group 1

The appropriate amount of vehicle was placed in a beaker. Daily aliquots were transferred into dosing containers and remaining vehicle into a labeled storage container. Aliquots and the storage container were stored at room temperature.

Groups 2-5

The formulations were prepared weekly. The bulk container of TBA was heated in a general-purpose lab oven to 300C to render the contents liquid and the requisite quantity of test article was weighed into a pre-warmed calibrated beaker. Approximately 90% of the total volume of warmed vehicle was added to the article and mixed on a magnetic stirrer until a clear solution had formed. The formulation was then brought up to the required volume and thoroughly re-mixed. Appropriate amounts of daily aliquots were taken and the remainder transferred into a labeled storage container with nitrogen cap, and stored at room temperature.

2.15. ANALYSIS OF DOSING FORMULATIONS

Formulation concentration and stability analyses were performed by the Huntingdon Life Sciences Analytical Chemistry Laboratory. As the

formulations comprised true aqueous solutions, homogeneity analysis was not necessary.

Trial formulations were prepared 8 days prior to the start of treatment, allowed to stand in sealed containers for 4 hours at room temperature, re-mixed by inversion and then sampled in duplicate (2 x 1 mL samples from each). One set of these 1 mL samples was analyzed for concentration using a method previously validated for the purpose. This analysis was intended to demonstrate 4-hour stability in support of daily formulation preparation. The duplicate set was retained frozen at -70°C or below as contingency, pending satisfactory outcome of the first analyses. The trial formulations were then stored at room temperature for 8 days, after which they were re-mixed by inversion and again sampled in duplicate. This second batch of samples was analyzed in parallel with samples taken from formulations used on the first day of dosing in the actual study. These results were intended to support weekly formulation preparation.

Dosing formulation samples (2 x 1 mL samples from each) were taken at the beginning and near the end of the dosing period in the study, and on a convenient occasion around the time of littering (total of 3 occasions). One set of 1 mL samples was analyzed initially, the duplicate set being retained as contingency, frozen at -70°C or below.

Any residual samples, and any reserved duplicate samples, were discarded following acceptance of the final analytical report.

2.16. TEST ARTICLE ADMINISTRATION

The dosing formulations were administered by gavage, using a suitably sized flexible catheter attached to an appropriately sized syringe. Dosing formulations were re-mixed by inversion prior to opening for dosing. Dosage volume (5 mL/kg body weight) was calculated for each animal using the most recent body weight recorded, except for F₀ females during the period of gestation after GD 17, when the dose volume remained fixed according to the GD 17 body weight until the animal had completed parturition. If at the time of dosing an animal had commenced parturition, but had not completed the process by approximately 1400 hours, it was not dosed that day. For females that had completed parturition, dosage volume reverted to being determined by the most recent body weight recorded, commencing with the weight recorded on PND 0 or PND 1, as appropriate.

2.17. EXPERIMENTAL EVALUATIONS

2.17.1. VIABILITY CHECKS (CAGE SIDE)

Observations for mortality, morbidity and signs of severe toxicity were made at least twice daily, prior to dosing during the treatment period, then again late in the work day. Any animal in extremely poor health or moribund condition was identified for further monitoring or possible euthanasia.

2.17.2. POST-DOSE OBSERVATIONS (CAGE-SIDE)

Each animal was checked for overt signs of toxicity prior to dosing and any changes from the preceding observation were recorded. Each dosed animal was then observed approximately one to two hours after dosing. An additional observation was made at approximately 4 hours after dosing, for the first 4 days of dosing only.

2.17.3. PHYSICAL EXAMINATIONS

The animals were examined cage-side and in the hand prior to randomization into the treatment groups, then once weekly through to terminal euthanasia, for any abnormality or sign of toxicity. Examinations included observations of general condition, skin and fur, eyes, nose, oral cavity, abdomen and external genitalia, occurrence of secretions and excretions, autonomic activity (*eg* lacrimation, piloerection, pupil size, unusual respiratory pattern). Changes in gait, posture and response to handling, the presence of clonic or tonic movements, stereotypy (*eg* excessive grooming, repetitive circling) or bizarre behavior (*eg* self-mutilation, walking backward) were recorded. During the treatment period this evaluation was performed prior to dosing, and for mated females it coincided with GD 0, 7, 14, 20 and PND 1, 7, 14 and 21.

2.17.4. BODY WEIGHTS

Body weights of the F₀ animals were recorded at the time of randomization into test groups, on the day treatment was initiated and weekly thereafter until pairing for mating. Males continued to be weighed weekly until termination, but for mated females weights were taken on GD 0, 7, 14, 17 and 20, and for those that

delivered litters, on PND 1, 4, 7, 14 and 21. F₀ female body weight was also recorded on PND 0, if the animal completed parturition. If the animal did not complete parturition and consequently was not dosed on that day, no PND 0 weight was recorded for that animal. Females without evidence of mating continued to be weighed weekly until termination, unless they delivered a litter.

Directly dosed F₁ offspring were weighed on PND 21, 24 and 28.

A terminal body weight (non-fasted) was also recorded for each F₀ and F₁ (post-weaning) animal.

Pre-weaning F₁ pups were weighed individually on PND 1, 4, 7, 14 and 21.

2.17.5. FEED CONSUMPTION

Feed consumption for the F₀ animals was recorded weekly during the 4-week pre-mating treatment period, but not during the mating (cohabitation) period. For mated females, feed consumption was recorded on GD 0-7, 7-14 and 14-20, and on PND 1-4, 4-7 and 7-14. Weekly measurements resumed for males after completion of the mating period, and also for any females without a sign of mating, until termination.

Feed consumption was measured for the cages of directly dosed F₁ offspring on PND 21-24 and 24-28.

2.17.6. PAIRING AND DETECTION OF MATING

Each female was transferred to the cage of a designated co-group male and remained there until positive evidence of mating was detected. Daily vaginal smears were taken each morning until either a copulatory plug was observed *in situ*, and/or sperm was detected in the smear, when the female was returned to its home cage. The maximum overall exposure to a male was 2 weeks, following which period the female was returned to its home cage.

The day of detection of a copulatory plug *in situ* and/or sperm in a vaginal smear was designated gestation day (GD) 0.

2.17.7. PARTURITION AND LACTATION

On GD 18, 3-5 days prior to expected parturition, mated females were transferred to solid, plastic cages with bedding material.

After GD 18, examination for signs of parturition was made twice daily (morning and afternoon). The day on which parturition was initiated was defined as postnatal day (PND) 0. The duration of gestation was deduced. Litters were observed as soon as possible after parturition for the number of live and dead pups, any pup abnormalities and the sex of each pup. All pups in the litter were uniquely identified by toe tattoo after parturition was complete. Thereafter, litters were observed twice daily (morning and afternoon). The presence of any dead pups was recorded and these were removed from the cage as found. Unusual observations, signs of deficient maternal care and any pups without milk in the stomach, were recorded.

On PND 4, each litter of more than ten pups was randomly culled to that number with sex distribution equalized where possible.

2.18. F₁ PUP EVALUATIONS

2.18.1. PUP PHYSICAL EXAMINATIONS

Each pup was given a gross physical examination and sexed on PND 0 (if parturition was complete), 1, 4 (pre-cull), 7, 14 and 21. The pups were also observed for any abnormal behavior.

2.18.2. BODY WEIGHTS

Individual pup body weights were recorded on PND 1, 4 (pre-cull), 7, 14 and 21.

2.19. SELECTION OF F₁ ANIMALS AT WEANING

From each litter, 2 males and 2 females were initially selected to secure the correct number of animals in case of possible losses early in the post-weaning dosing period. Of these, 1 male and 1 female offspring were used for subsequent direct treatment, while the second animal of each sex was available as a replacement. The extra animals that were not required were terminated on PND 23 or 28. Each group constituted a minimum of 10 offspring of each sex for dosing. Owing to a shortage of litters in Group 5

that could contribute the required number of pups, additional animals were selected from other available litters in the group as necessary.

2.20. TERMINAL EVALUATIONS

2.20.1. SCHEDULE FOR EUTHANASIA

F₀ males were terminated after at least 9 weeks of treatment. F₀ females with litters were terminated on PND 21. Females that mated but failed to deliver a litter were terminated at 25 to 26 days after evidence of mating. The single female that showed total litter loss before weaning was retained on treatment until it was clear that further mating in the study was not necessary, and then terminated as convenient (on its nominal PND 9).

Those offspring not selected for direct treatment were terminated on PND 21. Those offspring that were selected as reserves and not used for direct treatment were terminated on PND 23 or 28. The offspring used for direct treatment were terminated on PND 28.

2.20.2. METHODS OF EUTHANASIA

All post-weaning animals were euthanized by exposure to carbon dioxide. Pre-weanlings were euthanized by intraperitoneal injection of sodium pentobarbital.

2.20.3. F₀ ANIMALS – NECROPSY

A macroscopic necropsy was performed on all F₀ animals. This included examination of external surfaces, all orifices, cranial cavity, neck and its associated tissues and organs, thoracic, abdominal and pelvic cavities and their associated tissues and organs, and external surfaces of the brain. The number of implantation sites was recorded for each F₀ female. Apparently non-pregnant status was confirmed by ammonium sulphide staining (Salewski, 1964). Any gross lesions or tissues with significant findings were preserved in 10% neutral buffered formalin (NBF).

2.20.4. F₀ ANIMALS - ORGAN WEIGHTS

For all F₀ animals, the organs indicated below were removed at necropsy, carefully trimmed to remove fat and other contiguous tissue and were weighed as soon as possible after dissection to avoid drying. Paired organs were weighed separately.

Males	Females
Testes	Liver
Epididymides	Kidneys
Kidneys	
Liver	

2.20.5. F₀ MALES - SEMINOLOGY

For F₀ males at scheduled necropsy, the following sperm evaluations were performed by Pathology Associates International (PAI), Frederick, Maryland:

The right vas deferens was excised and placed in a pre-warmed solution of phosphate buffered saline and 1% Bovine Serum Albumin. After a minimum 3-minute "swim-out" period, a sample was placed in a Hamilton Thorne IVOS sperm analyzer and five microscope field images were stored electronically. For the Control and High dose groups, these fields were analyzed for percent motility.

The right testis and epididymis were frozen on dry ice for transport to PAI, Frederick, MD. These organs were stored frozen at -70°C or below until evaluation for sperm count (spermatids in the testis). For the Control and High dose groups only, the epididymis was thawed and the caudal portion removed and weighed. Homogenized samples of the caudal epididymis and the testis were stained and examined using a Hamilton Thorne IVOS sperm analyzer. For each stained preparation, 20 fields were counted. The total number of sperm in the caudal epididymis, or spermatids in the testis, were calculated and reported adjusted for organ weight. Additionally, two sperm morphology slides were prepared for each male, stained with Eosin and then evaluated for morphological development (at least 200 cells evaluated for each animal).

2.20.6. F₀ ANIMALS - TISSUES PRESERVED

Tissues listed in the following table were obtained at necropsy for all F₀ animals in each group and preserved in 10% neutral buffered formalin (NBF), with the exception of the testis, which was preserved in a modified Davidson's fixative for 48-72 hours and then stored in 10% neutral buffered formalin.

Tissue	Tissues Preserved	Microscopic Examination
Testis (1)	X	X
Epididymis (1)	X	X
Seminal vesicles (2) with coagulating gland	X	-
Prostate	X	-
Ovary (2) with oviducts	X	X
Thyroids with parathyroids	X	X
Kidneys (2)	X	-
All Macroscopic lesions/abnormalities	X	-

After fixation, the tissues and organs from all animals were routinely processed, embedded in paraffin, cut at a microtome setting of 4-7 microns, mounted on glass slides, stained with hematoxylin and eosin and examined by light microscopy.

2.20.7. F₀ ANIMALS - HISTOPATHOLOGY

Microscopic examinations for Control and High dose group F₀ animals were performed on the tissues and organs designated in the preceding table. During the microscopic examination of the testes, special attention was paid to the stages of spermatogenesis and interstitial testicular cell structure.

2.20.8. F₁ OFFSPRING: NON-SELECTED OFFSPRING AND DIRECTLY TREATED WEANLINGS

A necropsy was performed on all these animals. This included macroscopic examination of external surfaces, all orifices, cranial cavity, neck and its associated tissues and organs, thoracic, abdominal and pelvic cavities and their associated tissues and

organs, and external surfaces of the brain. Any gross lesions or tissues with significant findings were preserved in 10% NBF.

2.20.9. F₁ PUPS CULLED ON PND 4

A macroscopic external examination was performed for all F₁ pups culled on PND 4. Externally normal pups were discarded without necropsy (all were found to be apparently normal). Absence of milk in the stomach (presence/absence visible externally, through the skin) was noted.

2.20.10. F₁ PUPS - DECEDENTS PRIOR TO WEANING

A macroscopic external examination was performed for all F₁ pups found dead or sacrificed prior to weaning. A necropsy was performed where practical, including examination of the thoracic, abdominal and cranial contents for any grossly apparent abnormalities, but no tissues were preserved. Where possible, the presence or absence of milk in the stomach was determined.

2.21. STATISTICAL EVALUATIONS

2.21.1. CONTINUOUS DATA

Evaluation of equality of group means was made by an appropriate statistical method, followed by a multiple comparison test if needed. Bartlett's test (Bartlett, 1937) was performed to determine if group variances were equivalent. For all parameters the variances were equivalent, and parametric analysis procedures were used. The parametric method used was the standard one-way analysis of variance (ANOVA) using the F ratio to assess significance (Dunlap and Duffy, 1975). If significant differences among the means were indicated, additional tests were used to determine which means were significantly different from the control: Dunnett's (Dunlap et al., 19814). Bartlett's test for equality of variance was conducted at the 1% significance level; all other statistical tests were conducted at the 5% and 1% significance levels.

The following parameters were analyzed statistically:

Body weights

Body weight changes

Feed consumption values

Mean number of uterine implantations

F₁ pup weights, by sex and composite (each weighing interval during lactation)

Litter size

Organ weights and organ weight ratios

2.21.2. INCIDENCE DATA

A Fisher Exact Test with Bonferroni correction (Seigel, S, 1956) was performed to identify differences between control and treatment groups. All such tests were conducted at the 5% and 1%, two-sided risk levels.

The following parameters were analyzed:

Mortality incidence

Mating indices

Pregnancy rates

Fertility indices

(Note: Statistical analysis of pathological abnormalities was not necessary as there were no abnormalities present in the F₀ or F₁ treated animals).

2.22. DATA STORAGE

At the completion of the study, all reports, as well as the original study protocol, raw data, preserved specimens and retained samples produced by the Testing Facility or other contractor, will be maintained in the Testing Facility's Archives for a period of 1 year after issue of the signed final study report. The Sponsor will determine the subsequent disposition of these materials.

2.23. REGULATORY REFERENCES

2.23.1. TEST GUIDELINES

This study complied with or exceeded the Organization for Economic Cooperation and Development (July 27, 1995) OECD Guidelines for Testing of Chemicals, OECD Guideline 421: Reproduction/ Developmental Toxicity Screening Test.

2.23.2. GOOD LABORATORY PRACTICES

This study was conducted in compliance with EPA Good Laboratory Practices as set forth in 40 CFR Part 792 (TSCA) and Organization for Economic Cooperation and Development (OECD) Good Laboratory Practices as set forth in ENV/MC/CHEM (98) 17.

2.23.3. ANIMAL WELFARE ACT COMPLIANCE

This study complied with all appropriate parts of the Animal Welfare Act Regulations: 9 CFR Parts 1 and 2 Final Rules, Federal Register, Volume 54, No. 168, August 31, 1989, pp. 36112-36163 effective October 30, 1989 and 9 CFR Part 3 Animal Welfare Standards; Final Rule, Federal Register, Volume 56, No. 32, February 15, 1991, pp. 6426-6505 effective March 18, 1991.

2.24. PROTOCOL

The final protocol for this study is reproduced in Appendix HH.

2.25. PROTOCOL DEVIATIONS

The following protocol deviations occurred during the study, but were considered not to have compromised study validity or integrity.

1. Due to an oversight on 11 August 2003, PND 0 pup body weights were taken for all pups in Groups 2-5, not required by protocol. Therefore, these weights are not reported but are maintained in the Study File.
2. Kidney weights were taken together, instead of separately for Animal Numbers 1567 on presumed GD 26 and 2572 on presumed GD 25.
3. The right testis and right epididymis for Animal Numbers 3063 and 2069 were preserved in modified Davidson's/10% NBF, and the left testis and epididymis were frozen and sent to P.A.I., due to technician error.
4. Implantation sites were not recorded for Animal Numbers 2566 and 2570, owing to technician error.

5. When selecting F₁ weanlings for direct treatment, 2 of each sex (where available) were drawn initially from each available litter, instead of the 1 of each sex required by the protocol. This was to provide adequate reserves, against the possibility of losses soon after weaning.
6. A Certificate of Stability was not available, although required by the protocol. Correspondence from the Supplier indicated that the test article would be stable for at least one year from packaging.
7. F₁ pups were housed two or three per cage, by brother/sister, until termination on PND 28 and not by sex.
8. Due to an oversight, F₁ offspring pairs 2078/2578 and 2082/2582 had food consumption measured on Postnatal Days 22-24 rather than on Postnatal Days 21-24, as specified by the protocol.
9. Animal numbers 1563, 2573, 3570, 3572, 4563, 4564, 4568, 4572 and 4574 were dosed after 1400 following completion of delivery. However, this deviation occurred prior to the distribution of Protocol Amendment # 3, which specified that that if an animal had not completed delivery prior to 1400, they would not be dosed. After the amendment was issued, this procedure was followed.
10. The following reference of Seigel, S. 1956. Nonparametric Statistics for the Behavioral Sciences. McGraw-Hill, was utilized for statistical evaluation of incidence data but was not originally included in the protocol:
11. Animal Number 1567 was sacrificed on Gestation Day 26 although protocol references "the 25th day after last exposure to a male".

3. RESULTS

3.1. DOSE FORMULATION ANALYSIS

(Appendix A)

The stability of trial dose formulations covering the range 5-200 mg/ml was demonstrated. The analytical results obtained from samples of the solutions taken at the time of formulation and again after 8 days of storage at room temperature were effectively identical. As would be expected, there was no indication of any inhomogeneity of these solutions.

For the samples taken on 3 occasions during the dosing period of the study, achieved concentrations were all in the range 92-104% of nominal, indicating acceptable accuracy of formulation for the study.

3.2. F₀ MORTALITY

(Appendix B)

There was no intercurrent mortality during the study.

3.3. F₀ CLINICAL OBSERVATIONS

(Tables 2-4; Appendices C-F)

Animals in the High dose group (1000 mg/kg/day TBA) exhibited signs of apparent central nervous system (CNS) toxicity from the first day of dosing, characterized by unresponsiveness/lethargy and some ataxia. Some animals at this dose level also exhibited increased vocalization and rapid breathing. There was a lower incidence of similar findings among females (only) of the next highest dose group (400 mg/kg/day), occurring after approximately 2 weeks of dosing. All these effects were generally of moderate intensity among males, but only of mild intensity among females and only about half of the females in the 400 mg/kg/day group showed any discernible symptom. The effects generally appeared 1 to 2 hours after dosing and resolved within the 24-hour period intervening between doses.

While the effects at 1000 mg/kg/day remained at a broadly similar level of intensity during the study, those at 400 mg/kg/day became indiscernible after about the fourth week of dosing.

There were no such discernible clinical signs of toxicity at lower dosages of TBA. Some mild to moderate patchy alopecia, as well as some other minor findings, were recorded across all the groups in the study, but these findings are typical for the strain of animals and the incidences were not related to treatment.

A mass in the lower lip was detected in one female at 400 mg/kg/day during lactation. This lesion was confirmed at necropsy and was described as a tan coloured, firm mass of about 0.2 cm. in diameter. This finding was considered to have been incidental and not related to treatment.

3.4. F₀ BODY WEIGHT PERFORMANCE

(Tables 5-10; Appendices G-L)

Males in the High dose group (1000 mg/kg/day) showed reduced weight gain during the first week of treatment, leading to an approximate 5% deficit in body weight. This was not subsequently recovered, such that at termination after 9 weeks of treatment there was a 7% deficit as compared with Control. Although the deficit in initial body weight gain was statistically significant, the resulting differences in absolute weight were not. There was no effect on male body weight development at the lower dosages, and no meaningful effect on female body weight development at any of the dosages, until pregnancy was established.

TBA at the highest dose level (1000 mg/kg/day) resulted in decreased body weight gain in the last few days of gestation, leading to an approximate 6% deficit in body weight at gestation day (GD) 20 (just prior to parturition), as compared with Control and the other groups. Again, this absolute difference did not achieve statistical significance, although the difference in weight gain did so. The slight weight deficit remained for the High dose females after parturition was complete, but then recovered until in the third week of lactation these animals showed a net gain in weight, while the other groups lost some body weight (as normally occurs in late lactation, when there is a particularly high lactation demand on the female).

3.5. F₀ FEED CONSUMPTION**(Tables 11-13; Appendices M-0)**

Dosing with TBA did not cause any meaningful effect on feed consumption for either sex in the study, until the lactation period for the females at 1000 mg/kg/day. Consumption by these females over the first 2 weeks of lactation was approximately 15% reduced, as compared with the other groups. (Consumption was not measured over the last week of lactation, owing to the confounding influence of independent feeding by the offspring).

3.6. F₀ MATING PERFORMANCE, PREGNANCY RATE, DURATION OF GESTATION AND GESTATION INDEX**(Tables 14, 15 and Appendices P-R)**

There was no effect of TBA treatment on mating performance, all but 3 pairs (one pair in each of the Control, 64 and 160 mg/kg/day groups) mating at the first opportunity (first estrus). There was also no effect on the establishment of pregnancy, all groups having 11 or 12 pregnancies out of 12 pairings. All the pregnancies resulted in live litters. Thus, fertility and gestation indices were optimal or near optimal for both sexes at all dosages.

There was no unequivocal effect on gestation length. Half of the females at 1000 mg/kg/day and nearly half at 400 mg/kg/day had a gestation period of greater than 22 days (all but one of these shifts were to 23-day periods), while in the other groups there were not more than 2 females with periods of greater than 22 days. However, this shift remains within the normal range of gestation lengths for this strain (21-23 days, although with a distinct mode of 22).

3.7. F₁ LITTER SIZE, PUP SURVIVAL AND SEX RATIO**(Table 15 and Appendices R, S)**

There was no effect of TBA treatment on the number of implantations per pregnancy. However, there was a significant reduction in the number of live born per pregnancy at 1000 mg/kg/day, and an increase in the number of pups found to have been stillborn. The mean litter size for this group was then only 10 per litter on postnatal day (PND) 1, as compared with 14 or 15 in the other groups. Subsequently there was significantly reduced

pup survival at 1000 mg/kg/day, with only 80% survival to PND 4, as compared with close to 100% in the other groups. This was substantially contributed to by one early total litter loss in the group. After PND 4, however, pup survival was optimal or near optimal in all the groups. At the normal weaning date of PND 21, litter size at 1000 mg/kg/day was substantially reduced (by 50%) for 3 of the 10 surviving litters in the group, as a result of the early pup losses. There were no meaningful inter-group differences in live pup sex ratio for the litters.

3.8. F₁ CLINICAL OBSERVATIONS: LACTATION PERIOD
(Table 16 and Appendix T)

No treatment related clinical signs were observed among the pups during lactation.

3.9. F₁ BODY WEIGHTS: LACTATION PERIOD
(Tables 15, 17 and Appendix U)

F₁ offspring born to dams treated with TBA at 1000 mg/kg/day exhibited lower mean body weight than the Control offspring. For both sexes there was an approximate 10% deficit in weight at PND 1, increasing to approximately 15% by PND 7, at which point it achieved statistical significance. This deficit was still present at PND 14, but then decreased in late lactation such that by PND 21 the mean weight for males and females was about 11% and 6% less than Control, respectively.

3.10. F₁ DIRECTLY TREATED ANIMALS: CLINICAL OBSERVATIONS AND MORTALITY
(Table 18; Appendices V and W)

There were no clinical signs of toxicity, or mortality, among the offspring (either male or female) after direct TBA treatment at any of the dose levels.

3.11. F₁ DIRECTLY TREATED ANIMALS: BODY WEIGHT DEVELOPMENT

(Tables 19, 20; Appendices X and Y)

F₁ males and females born to dams treated with TBA at 1000 mg/kg/day during pregnancy and lactation, then directly treated with TBA daily at the same dose level from PND 21 to 27, exhibited lower mean body weight than the Control group. The initial differences from Control were approximately -13% and -6% for males and females, respectively, arising from the deficits acquired peri-natally. Direct TBA treatment then had no obvious further effect on body weight gain of either male or female offspring over the one-week direct dosing period after weaning. A single male pup in the High dose group did show substantially less weight gain than co-group animals.

3.12. F₁ DIRECTLY TREATED ANIMALS: FEED CONSUMPTION

(Table 21 and Appendix Z)

There was substantial loss of feed consumption data, owing to contamination of the feeder jars by the pups. It was not possible, therefore, to make unequivocal judgments for all the groups regarding the feed consumption patterns.

Generally, there appeared to have been no effect of direct TBA treatment on this parameter, although one cage of animals in the High dose group did show much-reduced consumption during the first three days of treatment (data from the subsequent 4 days was not obtained for this cage). The dosed pup in this cage (male # 5082) did show the lowest weight gain performance of the group.

3.13. F₀ NECROPSY FINDINGS

(Table 22 and Appendix BB)

There was a low, sporadic incidence of minor findings across the groups, none of which was related to TBA treatment.

3.14. F₀ ORGAN WEIGHTS

(Table 23 and Appendix AA)

There was a small increase in testis weight (about 8% in absolute terms, or 14% relative to body weight) at 1000 mg/kg/day, as compared with Control. The difference relative to body weight achieved statistical significance. However, testis weight is only weakly correlated with body weight over a wide range of body weights, and assessment of inter-group differences is generally best made by considering the absolute testis weight. The 8% increase in group mean testis weight at 1000 mg/kg/day, with a trend towards a lesser increase over Control at the lower dosages (not statistically significant), was considered to be of doubtful importance.

There was a dose related increase in male group mean kidney weight. At 1000 mg/kg/day the mean weight relative to body weight was increased by nearly 30%, as compared with Control. Over the dosage range 400 down to 64 mg/kg/day the difference from Control declined from about 15% to about 8%. Also in the 1000 mg/kg/day male group, mean liver weight (relative to body weight) was increased by about 15%, as compared with Control.

There was no evidence of a TBA treatment related effect on the female organ weights that were collected (kidneys and liver).

3.15. F₀ HISTOPATHOLOGY

(Table 24 and Appendix BB)

There were no microscopic findings in the reproductive tissues or thyroids associated with administration of TBA at 1000 mg/kg/day. The left testis of one animal in the 1000 mg/kg/day group contained a small number of tubules totally depleted of germ cells. Although none of the testes from the Control animals showed a similar finding, this is a relatively common background finding in rats of this strain and this single occurrence was considered incidental and unrelated to TBA treatment.

3.16. SEMINOLOGY

(Appendix EE)

A very marginal decrease in mean sperm motility at 1000 mg/kg/day achieved statistical significance, although the difference from Control was

only -3%. The counts of epididymal sperm, of testicular spermatids, and the incidences of sperm abnormalities, were similar in all groups.

The apparent difference from Control in sperm motility at the High dose level was considered not to be of importance. The value of 91% is considered to be consistent with the range of values typically seen for this strain of animals: In 9 studies conducted by this laboratory during the 2-year period preceding the present study, values of 89-96% mean motility were recorded for Control groups (ref. Appendix DD (b), Background Data).

3.17. F₁ NECROPSY FINDINGS

3.17.1. NON-SELECTED PUPS (PND 21)

(Table 25 and Appendix CC)

There was only a low, sporadic incidence of minor findings in the pups, whether found dead during lactation or killed at (or soon after) PND 21. These findings were typical for the strain and there was no relationship to treatment.

3.17.2. F₁ TREATED ANIMALS (PND 28)

(Table 26 and Appendix DD)

For the weanlings directly treated from PND 21-27, again there was only a low incidence of typical, sporadic findings at necropsy. These were incidental and not related to treatment.

4. DISCUSSION

In terms of effects of TBA on reproduction and development, unequivocal effects were confined to the 1000 mg/kg/day dose level. These were increased peri-natal mortality and deficient body weight development among offspring.

The importance of an increased incidence of gestation lengths greater than 22 days at both 1000 and 400 mg/kg/day was less certain, particularly as the actual shift in gestation length for individuals (by about one day, nominally) remained within the normal range for this strain of animal.

Increased length of gestation usually results in increased birth weight followed by enhanced weight gain, a difference that persists after weaning. These consequential body weight enhancements could compensate in some degree for any deficit in weight that might have been acquired pre-natally. This would reduce the magnitude (but not the importance) of that earlier developmental effect, or could mask the effect altogether. In the present study, the individual data indeed shows that the offspring weight development enhancements among those dams with 23-day gestation lengths at 1000 mg/kg/day abolished the deficit from Control in mean offspring weight by the time of weaning.

While offspring weight development among those dams with 21/22-day gestation lengths was reduced at 1000 mg/kg/day, at 400 mg/kg/day it was similar to Control and the other lower dosage groups. It is therefore improbable that the increased occurrence of 23-day gestation lengths in the 400 mg/kg/day group was masking any pre-existing offspring weight effect in that group, and it is safe to conclude that this dosage represents a no-adverse-effect level for offspring development (as indicated by body weight).

5. CONCLUSIONS

Daily treatment by gavage with TBA at 1000 mg/kg/day resulted in mild to moderate toxicity, and although there was no effect on mating performance or fertility, there was significant peri-natal mortality among the offspring. The body weight of live offspring was deficient at birth, as was their subsequent weight development during the first 2 post-natal weeks.

At 400 mg/kg/day, there was a lower incidence of transient mild toxicity in females only, commencing after approximately 2 weeks of treatment and becoming indiscernible after the 4th week of treatment. This dosage was considered to be a no-adverse-effect level (NOAEL) for reproductive/developmental toxicity.

It was considered that TBA at 160 mg/kg/day represented an overall NOAEL for this study.

There was no definite effect of direct dosing of offspring for one week after weaning at the same dose levels as were received by their respective parents.

CALCULATIONS

General Note:

Individual animal data values presented in this report may be rounded. Unrounded individual animal data values are used to calculate the reported mean and standard deviation values. Therefore, use of the reported individual values to reproduce means, standard deviations and/or to perform any subsequent calculations may produce minor discrepancies between the calculated values and those presented in this report.

Feed Consumption:

grams of feed consumed \div no. of days = grams/animal/day

Mating Index: (Mating - defined as female with vaginal sperm or vaginal plug or that gave birth to a litter)

Females – Number of females mated/number of females exposed to males

Males – Number of males with confirmed mating/number of males placed with females

Fertility Index:

Females – Number of females pregnant/number of females exposed to males

Males – Number of males with females pregnant/number of males placed with females

Pregnancy Index:

Number of females pregnant/number of females mated

Gestation Index:

Number of females with liveborn/number of females with confirmed pregnancy

Viability Index:

Number of pups alive on Lactation Day 4 [precull]/number of liveborn pups

CALCULATIONS

Lactation Index:

Number of pups alive on Lactation Day 21/number of pups alive on Lactation Day 4
[postcull]

Live Birth Index:

Total number of liveborn pups/total number of pups born

REFERENCES

Bartlett, M.S. 1937. Properties of sufficiency and statistical tests. Proceedings of the Royal Society, Series A, 160: 268-282

Dunlap, W.P. and Duffy, J.A. 1975. Fortran IV Functions for Calculating Exact Probabilities Associated with Z, Chi-Square, T and F Values. Behav. Res. Methods and Instrumentations 7:59-60

Dunlap, W.P., Marx, M.S. and Agamy, G.G. 1981. Fortran IV functions for calculating probabilities associated with Dunnett's test. Behav. Res. Methods and Instrumentation 13: 363-366

Salewski, V.E. (1964): Farbemethode zum makroskopischen nachweis von implantationsstellen am uterus der ratte. Naunyn-Schmeidebergs Archiv fur exper. Pathologic und Pharm., 247, 367

Seigel, S. 1956. Nonparametric Statistics for the Behavioral Sciences. McGraw-Hill

	General Preface	
--	-----------------	--

General Notes

1. The pre-mating period ends at Study Day 27.
2. 03-4254 "P" refers to the F₁ generation animals.

SUMMARY OF SURVIVAL AND PREGNANCY

No statistically significant differences

	Summary of Weekly Clinical Observations Preface	Table 2
--	--	---------

Number of animals examined represents the total number of animals observed and animals which were found dead, died accidentally or were killed in a moribund condition or at a scheduled sacrifice for a given interval.

Total represents a cumulative total of all animals with the indicated observation one or more times during the study.

Corresponding dose levels for each group were as follows:

Group I - 0 mg/kg/day
Group II - 64 mg/kg/day
Group III - 160 mg/kg/day
Group IV - 400 mg/kg/day
Group V - 1000 mg/kg/day

TABLE 2 - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

MALES

SUMMARY OF WEEKLY CLINICAL OBSERVATIONS

	GROUP#	DAY OF STUDY											TOTAL
		-5	6	13	20	27	34	41	48	55	62	64	
# OF ANIMALS EXAMINED	I	12	12	12	12	12	12	12	12	12	12	12	
	II	12	12	12	12	12	12	12	12	12	12	12	
	III	12	12	12	12	12	12	12	12	12	12	12	
	IV	12	12	12	12	12	12	12	12	12	12	12	
	V	12	12	12	12	12	12	12	12	12	12	12	
Normal													
WITHIN NORMAL LIMITS	I	12	11	9	10	10	9	10	10	10	10	0	12
	II	12	10	9	9	9	8	9	9	8	8	0	12
	III	12	11	11	10	10	10	10	9	9	9	0	12
	IV	12	12	10	8	7	7	7	7	7	6	0	12
	V	12	8	5	5	5	7	8	6	7	6	0	12
Dead													
TERMINAL SACRIFICE	I	0	0	0	0	0	0	0	0	0	0	12	12
	II	0	0	0	0	0	0	0	0	0	0	12	12
	III	0	0	0	0	0	0	0	0	0	0	12	12
	IV	0	0	0	0	0	0	0	0	0	0	12	12
	V	0	0	0	0	0	0	0	0	0	0	12	12
Gen. Appearance													
RED EXUDATE (GENERAL)	I	0	0	1	0	0	0	0	0	0	0	0	1
	II	0	0	0	0	0	0	0	0	0	0	0	0
	III	0	0	0	0	0	0	0	0	0	0	0	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0
	V	0	0	0	0	0	0	0	0	0	0	0	0
SWOLLEN PAW(S)													
	I	0	0	0	0	0	0	0	0	0	0	0	0
	II	0	0	0	0	0	0	0	0	0	0	0	0
	III	0	0	0	0	0	0	0	0	0	0	0	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0
	V	0	0	0	1	1	1	1	1	0	0	0	1

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

SUMMARY OF WEEKLY CLINICAL OBSERVATIONS

[illegible]

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

SUMMARY OF WEEKLY CLINICAL OBSERVATIONS

[illegible]

TABLE 2 - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

MALES

SUMMARY OF WEEKLY CLINICAL OBSERVATIONS

		DAY OF STUDY											
	GROUP#	-5	6	13	20	27	34	41	48	55	62	64	TOTAL
<hr/>													
# OF ANIMALS EXAMINED	I	12	12	12	12	12	12	12	12	12	12	12	
	II	12	12	12	12	12	12	12	12	12	12	12	
	III	12	12	12	12	12	12	12	12	12	12	12	
	IV	12	12	12	12	12	12	12	12	12	12	12	
	V	12	12	12	12	12	12	12	12	12	12	12	
<hr/>													
INCISORS BROKEN/MISSING	I	0	0	0	0	0	1	0	0	0	0	0	1
	II	0	0	0	0	0	1	0	0	0	0	0	1
	III	0	0	0	0	0	0	0	1	1	1	0	2
	IV	0	0	0	0	0	0	0	0	0	0	0	0
	V	0	0	0	0	0	0	0	0	0	0	0	0
<hr/>													
Behavior/Activity													
<hr/>													
INCREASED VOCALIZATION	I	0	0	0	0	0	0	0	0	0	0	0	0
	II	0	0	0	0	0	0	0	0	0	0	0	0
	III	0	0	0	0	0	0	0	0	0	0	0	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0
	V	0	1	3	4	4	3	2	3	3	4	0	5
<hr/>													
Respiration													
<hr/>													
RAPID BREATHING	I	0	0	0	0	0	0	0	0	0	0	0	0
	II	0	0	0	0	0	0	0	0	0	0	0	0
	III	0	1	1	0	0	0	0	0	0	0	0	1
	IV	0	0	0	0	0	0	0	0	0	0	0	0
	V	0	3	5	3	3	0	0	0	0	0	0	5
<hr/>													
RALES - MOIST	I	0	0	0	0	0	0	0	0	0	0	0	0
	II	0	0	0	0	0	0	0	0	0	0	0	0
	III	0	0	0	0	0	0	0	0	0	0	0	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0
	V	0	0	0	1	1	0	0	0	0	0	0	1

TABLE 2 - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

FEMALES

SUMMARY OF WEEKLY CLINICAL OBSERVATIONS

[illegible]

TABLE 2 - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

FEMALES

SUMMARY OF WEEKLY CLINICAL OBSERVATIONS

	GROUP#	DAY OF STUDY											TOTAL
		-5	6	13	20	27	34	41	48	55	62	64	
# OF ANIMALS EXAMINED	I	12	12	12	12	12	2	1	1	0	0	0	
	II	12	12	12	12	12	1	1	1	0	0	0	
	III	12	12	12	12	12	1	0	0	0	0	0	
	IV	12	12	12	12	12	0	0	0	0	0	0	
	V	12	12	12	12	12	0	0	0	0	0	0	
INCREASED ACTIVITY	I	0	0	0	0	0	0	0	0	0	0	0	0
	II	0	1	0	0	0	0	0	0	0	0	0	1
	III	0	2	1	0	0	0	0	0	0	0	0	3
	IV	0	3	0	0	0	0	0	0	0	0	0	3
	V	0	1	1	0	0	0	0	0	0	0	0	2
IRREGULAR GAIT	I	0	0	0	0	0	0	0	0	0	0	0	0
	II	0	0	0	0	0	0	0	0	0	0	0	0
	III	0	0	0	0	0	0	0	0	0	0	0	0
	IV	0	1	0	0	0	0	0	0	0	0	0	1
	V	0	0	0	0	0	0	0	0	0	0	0	0
INCREASED VOCALIZATION	I	0	0	0	0	0	0	0	0	0	0	0	0
	II	0	0	0	0	0	0	0	0	0	0	0	0
	III	0	0	0	0	0	0	0	0	0	0	0	0
	IV	0	0	1	0	0	0	0	0	0	0	0	1
	V	0	0	1	1	1	0	0	0	0	0	0	1
Respiration													
RAPID BREATHING	I	0	0	0	0	0	0	0	0	0	0	0	0
	II	0	0	0	0	0	0	0	0	0	0	0	0
	III	0	3	3	0	0	0	0	0	0	0	0	3
	IV	0	2	5	3	2	0	0	0	0	0	0	6
	V	0	1	3	1	1	0	0	0	0	0	0	3

TABLE 3 - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

SUMMARY OF CLINICAL OBSERVATIONS DURING GESTATION - (frequency/animals)

	DOSE GROUP: DOSE LEVEL (MG/KG/DAY):	1 0	2 64	3 160	4 400	5 1000
DAY 0 to 20						
Normal						

WITHIN NORMAL LIMITS		32/10	36/10	48/12	38/10	38/10
Dermal-General						

ALOPECIA - EXTREMITIES/SNOUT		12/ 4	3/ 2	0/ 0	8/ 2	10/ 3
ALOPECIA - GENERAL		0/ 0	1/ 1	0/ 0	0/ 0	0/ 0
Ocular						

CHROMODACRYORRHEA - UNILATERAL		0/ 0	4/ 1	0/ 0	0/ 0	0/ 0
LACRIMATION - UNILATERAL		0/ 0	2/ 1	0/ 0	0/ 0	0/ 0
Oral/Buccal						

INCISORS MALOCCLUDED		0/ 0	4/ 1	0/ 0	0/ 0	0/ 0
INCISORS BROKEN/MISSING		0/ 0	0/ 0	0/ 0	1/ 1	0/ 0
Respiration						

RAPID BREATHING		0/ 0	0/ 0	0/ 0	1/ 1	0/ 0

TABLE 4 - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

SUMMARY OF MATERNAL CLINICAL OBSERVATIONS DURING LACTATION - (frequency/animals)

	DOSE GROUP: DOSE LEVEL (MG/KG/DAY):	1 0	2 64	3 160	4 400	5 1000
DAY 1 to 21						
Normal						
WITHIN NORMAL LIMITS		33/ 9	31/ 9	48/12	35/10	25/ 7
TERMINAL SACRIFICE		11/11	11/11	12/12	12/12	11/11
Dermal-General						
ALOPECIA - EXTREMITIES/SNOUT		11/ 3	9/ 3	0/ 0	13/ 4	17/ 5
Ocular						
CHROMODACRYORRHEA - UNILATERAL		0/ 0	4/ 1	0/ 0	0/ 0	0/ 0
Oral/Buccal						
INCISORS MALOCCLUDED		0/ 0	4/ 1	0/ 0	0/ 0	0/ 0
INCISORS BROKEN/MISSING		0/ 0	2/ 1	0/ 0	0/ 0	0/ 0
Palpable masses						
MASS BOTTOM LIP		0/ 0	0/ 0	0/ 0	1/ 1	0/ 0

TABLE 5 - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

MALES			MEAN BODY WEIGHT VALUES (GRAMS)				
			1	2	3	4	5
DOSE GROUP:			0	64	160	400	1000
DOSE LEVEL (MG/KG/DAY):							
DAY -5		MEAN	230	231	231	230	230
		S.D.	9.0	9.6	9.7	9.9	9.6
		N	12	12	12	12	12
DAY 0		MEAN	274	276	273	275	272
		S.D.	12.2	10.9	13.4	14.2	12.8
		N	12	12	12	12	12
DAY 6		MEAN	314	317	311	314	299
		S.D.	17.1	14.7	18.6	18.5	13.4
		N	12	12	12	12	12
DAY 13		MEAN	356	361	353	357	340
		S.D.	23.5	19.0	21.8	20.0	16.9
		N	12	12	12	12	12
DAY 20		MEAN	391	396	386	391	374
		S.D.	29.9	22.0	26.0	22.3	23.8
		N	12	12	12	12	12
DAY 27		MEAN	424	428	418	424	401
		S.D.	35.6	24.2	29.3	23.6	24.4
		N	12	12	12	12	12
DAY 34		MEAN	442	442	436	443	420
		S.D.	39.9	26.5	27.9	21.9	26.6
		N	12	12	12	12	12
DAY 41		MEAN	475	471	462	473	446
		S.D.	43.5	29.2	28.7	26.3	34.1
		N	12	12	12	12	12
DAY 48		MEAN	497	491	479	494	463
		S.D.	45.8	31.3	27.1	27.4	37.7
		N	12	12	12	12	12
DAY 55		MEAN	516	510	498	512	483
		S.D.	48.3	32.3	30.6	29.2	37.4
		N	12	12	12	12	12

No statistically significant differences

5-FEB-2004 11:41

Huntingdon Life Sciences 03-4254

PAGE 56

TABLE 5 - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

MALES

MEAN BODY WEIGHT VALUES (GRAMS)

		1	2	3	4	5
DOSE GROUP:		1	2	3	4	5
DOSE LEVEL (MG/KG/DAY):		0	64	160	400	1000
DAY 62						
	MEAN	536	527	515	527	498
	S.D.	50.1	32.3	33.9	31.9	37.6
	N	12	12	12	12	12

No statistically significant differences

TABLE 5 - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

FEMALES			MEAN BODY WEIGHT VALUES (GRAMS)				
			1	2	3	4	5
DOSE GROUP:			0	64	160	400	1000
DOSE LEVEL (MG/KG/DAY):							
DAY -5		MEAN	180	180	180	179	180
		S.D.	8.7	8.0	10.6	9.0	8.6
		N	12	12	12	12	12
DAY 0		MEAN	199	201	198	199	202
		S.D.	11.2	12.4	13.9	11.0	13.5
		N	12	12	12	12	12
DAY 6		MEAN	216	219	210	209	210
		S.D.	16.0	17.4	17.6	15.2	13.5
		N	12	12	12	12	12
DAY 13		MEAN	224	236	224	223	221
		S.D.	18.5	21.2	19.8	16.7	16.2
		N	12	12	12	12	12
DAY 20		MEAN	237	244	234	236	237
		S.D.	18.1	19.8	22.2	19.2	20.2
		N	12	12	12	12	12
DAY 27		MEAN	245	252	244	244	247
		S.D.	18.5	22.3	23.7	21.3	23.9
		N	12	12	12	12	12

No statistically significant differences

TABLE 6 - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

MALES			MEAN BODY WEIGHT GAIN (GRAMS)					
			DOSE GROUP:	1	2	3	4	5
			DOSE LEVEL (MG/KG/DAY):	0	64	160	400	1000
DAY	-5 TO	0	MEAN	44	45	43	45	42
			S.D.	5.0	3.7	6.0	5.9	5.1
			N	12	12	12	12	12
DAY	0 TO	6	MEAN	41	42	38	39	27**
			S.D.	6.0	4.5	7.6	6.1	8.0
			N	12	12	12	12	12
DAY	6 TO	13	MEAN	42	43	41	44	41
			S.D.	8.5	5.9	4.8	8.2	6.5
			N	12	12	12	12	12
DAY	13 TO	20	MEAN	35	36	33	33	34
			S.D.	8.2	4.1	9.3	4.1	9.4
			N	12	12	12	12	12
DAY	20 TO	27	MEAN	33	32	32	33	26*
			S.D.	7.4	4.2	6.0	3.9	4.5
			N	12	12	12	12	12
DAY	27 TO	34	MEAN	18	14	18	19	19
			S.D.	8.7	6.8	4.8	5.4	6.0
			N	12	12	12	12	12
DAY	34 TO	41	MEAN	33	29	26	30	26
			S.D.	4.3	6.5	4.4	8.2	9.5
			N	12	12	12	12	12

Statistical key: * = p<0.05 ** = p<0.01

TABLE 6 - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

MALES			MEAN BODY WEIGHT GAIN (GRAMS)				
			1	2	3	4	5
DOSE GROUP:			0	64	160	400	1000
DOSE LEVEL (MG/KG/DAY) :							
DAY 41 TO 48	MEAN		22	19	17	21	17
	S.D.		5.3	3.4	4.4	3.8	6.9
	N		12	12	12	12	12
DAY 48 TO 55	MEAN		19	19	20	18	20
	S.D.		6.7	4.2	7.1	7.3	5.9
	N		12	12	12	12	12
DAY 55 TO 62	MEAN		20	17	17	15	16
	S.D.		4.2	3.8	4.6	7.2	9.2
	N		12	12	12	12	12
DAY 0 TO 62	MEAN		262	252	242	252	226
	S.D.		42.4	23.2	24.9	26.6	34.8
	N		12	12	12	12	12

No statistically significant differences

TABLE 6 - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

FEMALES				MEAN BODY WEIGHT GAIN (GRAMS)				
DOSE GROUP:				1	2	3	4	5
DOSE LEVEL (MG/KG/DAY) :				0	64	160	400	1000
DAY	-5 TO	0	MEAN	19	21	18	20	22
			S.D.	5.3	6.2	6.4	5.4	8.4
			N	12	12	12	12	12
DAY	0 TO	6	MEAN	17	18	13	10	8*
			S.D.	7.3	9.9	8.7	9.0	5.4
			N	12	12	12	12	12
DAY	6 TO	13	MEAN	8	17	14	14	11
			S.D.	9.9	11.3	7.5	9.4	9.2
			N	12	12	12	12	12
DAY	13 TO	20	MEAN	13	8	9	12	16
			S.D.	6.1	14.2	9.7	9.7	8.2
			N	12	12	12	12	12
DAY	20 TO	27	MEAN	8	8	10	8	9
			S.D.	5.4	7.1	5.0	7.9	7.5
			N	12	12	12	12	12
DAY	0 TO	27	MEAN	46	51	46	45	45
			S.D.	9.2	12.5	12.1	13.1	15.0
			N	12	12	12	12	12

Statistical key: * = p<0.05

TABLE 7 - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

SUMMARY OF GESTATION BODY WEIGHTS (GRAMS)

DOSE GROUP:		1	2	3	4	5
DOSE LEVEL (MG/KG/DAY):		0	64	160	400	1000
DAY 0	MEAN	253	259	251	254	255
	S.D.	22.8	22.4	22.7	23.8	17.0
	N	10	10	12	12	11
DAY 7	MEAN	291	296	288	292	286
	S.D.	23.1	24.6	27.6	23.7	21.8
	N	10	10	12	12	11
DAY 14	MEAN	327	334	320	333	321
	S.D.	25.4	27.3	32.2	25.7	20.4
	N	10	10	12	12	11
DAY 17	MEAN	356	359	350	360	347
	S.D.	26.1	29.7	36.0	28.2	24.6
	N	10	10	12	12	11
DAY 20	MEAN	402	402	393	402	379
	S.D.	28.0	32.4	41.2	31.9	26.7
	N	10	10	12	12	11

No statistically significant differences

TABLE 8 - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

		SUMMARY OF GESTATION BODY WEIGHT GAIN (GRAMS)				
DOSE GROUP:		1	2	3	4	5
DOSE LEVEL (MG/KG/DAY):		0	64	160	400	1000
DAYS 0 TO 7	MEAN	38	37	36	38	31
	S.D.	7.3	6.6	8.5	7.2	10.5
	N	10	10	12	12	11
DAYS 7 TO 14	MEAN	36	38	33	41	34
	S.D.	6.8	5.1	7.0	7.0	5.5
	N	10	10	12	12	11
DAYS 14 TO 17	MEAN	29	26	29	27	26
	S.D.	4.3	4.9	5.7	5.9	5.8
	N	10	10	12	12	11
DAYS 17 TO 20	MEAN	46	43	43	42	32**
	S.D.	10.3	6.5	11.5	8.4	7.6
	N	10	10	12	12	11
DAYS 0 TO 20	MEAN	148	143	142	148	124*
	S.D.	16.3	13.3	25.5	18.5	16.8
	N	10	10	12	12	11

Statistical key: * = p<0.05 ** = p<0.01

TABLE 9 - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS.

SUMMARY OF MATERNAL LACTATION BODY WEIGHTS (GRAMS)

		1	2	3	4	5
DOSE GROUP:						
DOSE LEVEL (MG/KG/DAY):		0	64	160	400	1000
DAY 0	MEAN	303	313	299	304	282
	S.D.	26.7	19.0	31.2	27.4	30.1
	N	9	9	11	11	7
DAY 1	MEAN	301	301	298	302	281
	S.D.	20.2	28.7	27.9	25.4	22.6
	N	11	11	12	12	11
DAY 4	MEAN	318	315	310	317	296
	S.D.	20.8	25.8	32.5	31.5	24.4
	N	11	11	12	12	10
DAY 7	MEAN	323	329	319	329	315
	S.D.	20.8	28.8	30.2	29.2	27.6
	N	11	11	12	12	10
DAY 14	MEAN	347	348	338	352	336
	S.D.	22.1	30.7	28.9	28.1	33.3
	N	11	11	12	12	10
DAY 21	MEAN	332	333	326	334	346
	S.D.	18.2	30.9	26.8	25.1	24.2
	N	11	11	12	12	10

No statistically significant differences

TABLE 10 - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

SUMMARY OF MATERNAL LACTATION BODY WEIGHT GAIN (GRAMS)

DOSE GROUP: DOSE LEVEL (MG/KG/DAY):		1 0	2 64	3 160	4 400	5 1000
DAYS 1 TO 4	MEAN	16	14	11	15	12
	S.D.	9.4	8.5	9.4	10.5	7.3
	N	11	11	12	12	10
DAYS 4 TO 7	MEAN	6	13	9	11	18
	S.D.	15.5	8.2	7.2	9.2	5.8
	N	11	11	12	12	10
DAYS 7 TO 14	MEAN	23	19	19	24	22
	S.D.	12.2	9.9	10.2	5.3	17.3
	N	11	11	12	12	10
DAYS 14 TO 21	MEAN	-15	-14	-12	-18	10**
	S.D.	13.6	7.9	17.0	11.3	17.9
	N	11	11	12	12	10
DAYS 1 TO 21	MEAN	31	32	28	32	62**
	S.D.	14.5	11.9	17.4	13.6	14.7
	N	11	11	12	12	10

Statistical key: ** = p<0.01

TABLE 11 - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

MALES			MEAN FEED CONSUMPTION (GRAMS/ANIMAL/DAY)				
DOSE GROUP: DOSE LEVEL (MG/KG/DAY):			1 0	2 64	3 160	4 400	5 1000
DAY 6	MEAN		26	27	26	27	25
	S.D.		2.0	1.8	2.0	1.8	1.7
	N		12	12	12	12	12
DAY 13	MEAN		25	27	25	26	26
	S.D.		2.1	2.2	2.3	1.8	1.9
	N		11	9	10	11	11
DAY 20	MEAN		27	28	26	28	27
	S.D.		2.7	2.2	3.1	1.9	1.9
	N		12	12	11	12	12
DAY 27	MEAN		27	28	28	29	28
	S.D.		2.6	2.0	3.5	1.9	1.8
	N		12	8	12	12	12
DAY 48	MEAN		28	27	27	28	28
	S.D.		2.6	2.0	2.2	2.4	2.0
	N		12	12	11	12	12
DAY 55	MEAN		27	27	27	28	28
	S.D.		2.0	2.0	2.1	1.8	2.1
	N		12	12	11	12	12
DAY 62	MEAN		28	28	28	28	28
	S.D.		2.2	1.6	2.5	1.9	1.8
	N		12	12	12	12	12

No statistically significant differences

TABLE 11 - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

FEMALES			MEAN FEED CONSUMPTION (GRAMS/ANIMAL/DAY)				
			1	2	3	4	5
DOSE LEVEL (MG/KG/DAY):			0	64	160	400	1000
DAY 6		MEAN	18	20*	19	19	18
		S.D.	1.5	2.4	1.3	1.7	1.1
		N	11	11	11	12	9
DAY 13		MEAN	18	20	18	18	18
		S.D.	1.8	3.3	1.9	1.7	0.9
		N	12	7	11	12	10
DAY 20		MEAN	20	20	18	19	20
		S.D.	4.9	3.2	1.3	1.8	1.4
		N	12	12	12	12	10
DAY 27		MEAN	19	18	18	19	20
		S.D.	4.6	2.2	1.0	1.8	1.8
		N	11	8	10	12	11

Statistical key: * = p<0.05

TABLE 12 - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

SUMMARY OF GESTATION FEED CONSUMPTION (GRAMS/ANIMAL/DAY)

DOSE GROUP:		1	2	3	4	5
DOSE LEVEL (MG/KG/DAY):		0	64	160	400	1000
DAYS 0 TO 7	MEAN	23	24	23	23	23
	S.D.	1.8	2.2	2.2	2.0	2.7
	N	10	9	12	11	8
DAYS 7 TO 14	MEAN	24	25	25	25	24
	S.D.	2.0	2.3	2.4	2.5	2.8
	N	10	9	11	12	10
DAYS 14 TO 20	MEAN	24	25	25	26	25
	S.D.	1.6	2.1	2.4	2.5	2.9
	N	10	8	12	10	9
DAYS 0 TO 20	MEAN	24	24	24	25	24
	S.D.	1.6	1.9	2.3	2.2	2.6
	N	10	10	12	12	10

No statistically significant differences

TABLE 13 - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

SUMMARY OF LACTATION FEED CONSUMPTION (GRAMS/ANIMAL/DAY)

DOSE GROUP:		1	2	3	4	5
DOSE LEVEL (MG/KG/DAY):		0	64	160	400	1000
DAYS 1 TO 4	MEAN	37	35	35	36	29
	S.D.	5.3	4.6	8.2	8.1	7.2
	N	11	11	12	12	10
DAYS 4 TO 7	MEAN	46	47	46	50	43
	S.D.	5.4	4.7	7.8	5.2	9.1
	N	8	10	10	12	10
DAYS 7 TO 14	MEAN	62	61	57	62	52*
	S.D.	4.5	8.6	10.9	4.9	10.3
	N	11	11	10	11	10
DAYS 1 TO 14	MEAN	49	48	46	49	41
	S.D.	4.7	5.9	7.9	5.8	8.2
	N	11	11	12	12	10

Statistical key: * = p<0.05

TABLE 14 - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

SUMMARY OF COHABITATION DATA

DOSE GROUP: DOSE LEVEL (MG/KG/DAY):		1 0	2 64	3 160	4 400	5 1000
Females paired with males	N	12	12	12	12	12
Total number mated	N	12	12	12	12	12
female mating index	%	100.0	100.0	100.0	100.0	100.0
pregnant	N	11	11	12	12	11
female fertility index	%	91.7	91.7	100.0	100.0	91.7
pregnancy index	%	91.7	91.7	100.0	100.0	91.7
Males placed with females	N	12	12	12	12	12
Total number mated	N	12	12	12	12	12
male mating index	%	100.0	100.0	100.0	100.0	100.0
with females pregnant	N	11	11	12	12	11
male fertility index	%	91.7	91.7	100.0	100.0	91.7
Females with defined day 0 of Gestation	N	11	11	12	12	12
No. of days until Mating	MEAN	2.3	2.7	3.1	3.3	3.2
	S.D.	1.79	1.56	2.64	0.87	1.47
Day 1 to 4	N	10	10	9	11	9
	%	90.9	90.9	75.0	91.7	75.0
Day 5 to 8	N	1	1	2	1	3
	%	9.1	9.1	16.7	8.3	25.0
Day 9 to 14	N	0	0	1	0	0
	%	0.0	0.0	8.3	0.0	0.0

No statistically significant differences

Huntingdon Life Sciences 03-4254

TABLE 15 - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

		SUMMARY OF DELIVERY AND LITTER DATA				
DOSE GROUP: DOSE LEVEL (MG/KG/DAY):		1 0	2 64	3 160	4 400	5 1000
Females on Study	N	12	12	12	12	12
Females Mated	N	12	12	12	12	12
Mating Index	%	100.0	100.0	100.0	100.0	100.0
Females Pregnant	N	11	11	12	12	11
Female Fertility Index	%	91.7	91.7	100.0	100.0	91.7
Females with Liveborn	N	11	11	12	12	11
Gestation Index	%	100.0	100.0	100.0	100.0	100.0
Females Completing Delivery	N	11	11	12	12	11
	%	100.0	100.0	100.0	100.0	100.0
with Stillborn Pups	N	3	1	2	2	4
	%	27.3	9.1	16.7	16.7	36.4
with all Stillborn	N	0	0	0	0	0
	%	0.0	0.0	0.0	0.0	0.0
Litters with Liveborn, but no Pups Alive						
day 4	N	0	0	0	0	1
	%	0.0	0.0	0.0	0.0	9.1
day 21	N	0	0	0	0	1
	%	0.0	0.0	0.0	0.0	9.1
Duration of Gestation	MEAN	21.9	21.9	22.2	22.3	22.5
	S.D.	0.32	0.57	0.72	0.65	0.52
	N	10	10	12	12	11

No statistically significant differences

Huntingdon Life Sciences 03-4254

TABLE 15 - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

SUMMARY OF DELIVERY AND LITTER DATA						
DOSE GROUP: DOSE LEVEL (MG/KG/DAY):		1 0	2 64	3 160	4 400	5 1000
Litters with Liveborn Pups	N	11	11	12	12	11
Pups Delivered (total)	N	172	154	169	174	153
	MEAN	15.6	14.0	14.1	14.5	13.9
	S.D.	1.50	2.00	3.40	2.24	2.43
Liveborn	N	169	153	165	170	147
Live Birth Index	%	98.3	99.4	97.6	97.7	96.1
Stillborn	N	3	1	4	4	6
	%	1.7	0.6	2.4	2.3	3.9
Culled day 4		53	42	50	49	24
Liveborn, not culled prior to day 21	N	116	111	115	121	123
Pups Dying, Missing, and/or Cannibalized day 0	N	2	1	1	0	6
	%	1.2	0.7	0.6	0.0	4.1
days 1-4	N	4	1	2	1	32**
	%	2.4	0.7	1.2	0.6	21.8
days 5-21	N	0	0	0	1	1
	%	0.0	0.0	0.0	0.6	0.7
days 0-4	N	6	2	3	1	38**
	%	3.6	1.3	1.8	0.6	25.9
days 0-21	N	6	2	3	2	39**
	%	3.6	1.3	1.8	1.2	26.5
Pups Surviving 4 days Viability Index	N	163	151	162	169	109**
	%	96.4	98.7	98.2	99.4	74.1
Pups Surviving 21 days Lactation Index	N	110	109	112	119	84
	%	100.0	100.0	100.0	99.2	98.8

Statistical key: ** = p<0.01

Huntingdon Life Sciences 03-4254

TABLE 15 - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

		SUMMARY OF DELIVERY AND LITTER DATA				
DOSE GROUP: DOSE LEVEL (MG/KG/DAY):		1 0	2 64	3 160	4 400	5 1000
Implantation Sites per Litter	N	179	136 ^a	183	193	177
	MEAN	16.3	15.1	15.3	16.1	16.1
	S.D.	1.62	2.67	3.57	1.51	1.04
Live Pups/Litter day 1	MEAN	15.2	13.8	13.5	14.1	10.2**
	S.D.	1.25	1.99	3.99	2.39	5.12
	N	11	11	12	12	11
day 4 preculling	MEAN	14.8	13.7	13.5	14.1	9.9**
	S.D.	1.47	2.05	3.99	2.39	5.26
	N	11	11	12	12	11
day 4 postculling	MEAN	10.0	9.9	9.3	10.0	7.7*
	S.D.	0.00	0.30	2.31	0.00	3.32
	N	11	11	12	12	11
day 7	MEAN	10.0	9.9	9.3	10.0	7.6*
	S.D.	0.00	0.30	2.31	0.00	3.38
	N	11	11	12	12	11
day 14	MEAN	10.0	9.9	9.3	9.9	7.6*
	S.D.	0.00	0.30	2.31	0.29	3.38
	N	11	11	12	12	11
day 21	MEAN	10.0	9.9	9.3	9.9	7.6*
	S.D.	0.00	0.30	2.31	0.29	3.38
	N	11	11	12	12	11
Sex Ratio - Male Pups:Total Pups						
day 0	N	92	80	84	91	76
	%	54.4	52.3	50.9	53.5	52.1
day 21	N	55	55	57	60	43
	%	50.0	50.5	50.9	50.4	51.2

Statistical key: * = p<0.05 ** = p<0.01

^aThe uteri of animals 2566 (13 pups) and 2570 (14 pups) were not examined for implantation scars.

Huntingdon Life Sciences 03-4254

TABLE 15 - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

SUMMARY OF DELIVERY AND LITTER DATA						
DOSE GROUP:		1	2	3	4	5
DOSE LEVEL (MG/KG/DAY):		0	64	160	400	1000

Pup Weight/Litter (grams)						
day 1	MEAN	7.1	7.5	7.4	7.6	6.4
	S.D.	0.41	0.71	0.85	0.82	0.72
	N	11	11	12	12	11
day 4 preculling	MEAN	10.4	10.7	10.6	10.7	9.1
	S.D.	0.85	0.87	1.56	1.51	1.51
	N	11	11	12	12	10
day 4 postculling	MEAN	10.3	10.8	10.6	10.6	9.1
	S.D.	0.83	0.88	1.54	1.53	1.52
	N	11	11	12	12	10
day 7	MEAN	16.6	17.0	16.7	16.6	14.0**
	S.D.	1.13	1.53	2.39	1.95	2.08
	N	11	11	12	12	10
day 14	MEAN	32.6	32.0	31.7	32.1	27.5**
	S.D.	1.88	2.96	4.06	3.17	3.98
	N	11	11	12	12	10
day 21	MEAN	53.1	53.0	52.8	53.6	48.7
	S.D.	3.10	4.92	6.99	5.77	6.21
	N	11	11	12	12	10

Statistical key: ** = p<0.01

TABLE 16 - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

SUMMARY OF PUP CLINICAL OBSERVATIONS DURING LACTATION - (frequency/animals)

	DOSE GROUP: DOSE LEVEL (MG/KG/DAY):	1 0	2 64	3 160	4 400	5 1000
DAY 0 to 21						
Normal						

WITHIN NORMAL LIMITS		797/11	749/11	824/12	845/12	568/11
Gen. Appearance						

TOE APPEARS DAMAGED		0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
DIGIT MISSING		0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
Dermal-General						

ALOPECIA - EXTREMITIES/SNOUT		0/ 0	7/ 1	0/ 0	0/ 0	0/ 0
ALOPECIA - GENERAL		0/ 0	0/ 0	0/ 0	10/ 1	0/ 0
SCABS		0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
Pup observations						

PALE		0/ 0	0/ 0	1/ 1	0/ 0	0/ 0
ULCERATION		0/ 0	0/ 0	0/ 0	0/ 0	2/ 1

TABLE 17 - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

SUMMARY OF MEAN PUP BODY WEIGHTS (GRAMS)

DOSE GROUP: DOSE LEVEL (MG/KG/DAY):			1 0	2 64	3 160	4 400	5 1000
day 1 males	MEAN		7.3	7.7	7.4	7.7	6.5
	S.D.		0.42	0.70	0.69	0.84	0.86
	N		11	11	11	12	11
1 females	MEAN		6.9	7.3	7.1	7.4	6.3
	S.D.		0.41	0.73	0.88	0.79	0.71
	N		11	11	12	12	10
1 males+females	MEAN		7.1	7.5	7.4	7.6	6.4
	S.D.		0.41	0.71	0.85	0.82	0.72
	N		11	11	12	12	11
day 4 males preculling	MEAN		10.6	10.9	10.5	10.8	9.4
	S.D.		0.87	0.88	1.27	1.52	1.53
	N		11	11	11	12	9
4 females preculling	MEAN		10.1	10.5	10.3	10.5	9.2
	S.D.		0.87	0.89	1.58	1.47	1.33
	N		11	11	12	12	9
4 males+females preculling	MEAN		10.4	10.7	10.6	10.7	9.1
	S.D.		0.85	0.87	1.56	1.51	1.51
	N		11	11	12	12	10
day 4 males postculling	MEAN		10.5	11.0	10.5	10.7	9.4
	S.D.		0.83	0.88	1.24	1.56	1.55
	N		11	11	11	12	9
4 females postculling	MEAN		10.0	10.5	10.3	10.4	9.2
	S.D.		0.91	0.94	1.57	1.48	1.33
	N		11	11	12	12	9
4 males+females postculling	MEAN		10.3	10.8	10.6	10.6	9.1
	S.D.		0.83	0.88	1.54	1.53	1.52
	N		11	11	12	12	10

No statistically significant differences

TABLE 17 - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

SUMMARY OF MEAN PUP BODY WEIGHTS (GRAMS)

DOSE GROUP: DOSE LEVEL (MG/KG/DAY):		1 0	2 64	3 160	4 400	5 1000
day 7 males	MEAN	17.0	17.4	16.6	16.8	14.3**
	S.D.	1.13	1.63	2.17	1.99	2.26
	N	11	11	11	12	9
7 females	MEAN	16.3	16.6	16.3	16.4	14.1*
	S.D.	1.25	1.50	2.41	1.91	1.92
	N	11	11	12	12	9
7 males+females	MEAN	16.6	17.0	16.7	16.6	14.0**
	S.D.	1.13	1.53	2.39	1.95	2.08
	N	11	11	12	12	10
day 14 males	MEAN	33.3	32.6	31.4	32.6	27.6**
	S.D.	2.00	3.19	3.41	3.23	4.15
	N	11	11	11	12	9
14 females	MEAN	31.8	31.4	31.2	31.6	27.8
	S.D.	2.05	2.86	4.09	3.15	3.56
	N	11	11	12	12	9
14 males+females	MEAN	32.6	32.0	31.7	32.1	27.5**
	S.D.	1.88	2.96	4.06	3.17	3.98
	N	11	11	12	12	10
day 21 males	MEAN	54.6	54.2	52.9	54.7	48.8
	S.D.	3.37	4.77	6.66	6.39	5.99
	N	11	11	11	12	9
21 females	MEAN	51.6	51.7	51.8	52.4	48.7
	S.D.	3.07	5.20	7.06	5.30	6.60
	N	11	11	12	12	9
21 males+females	MEAN	53.1	53.0	52.8	53.6	48.7
	S.D.	3.10	4.92	6.99	5.77	6.21
	N	11	11	12	12	10

Statistical key: * = p<0.05 ** = p<0.01

TABLE 17 - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

SUMMARY OF PUP BODY WEIGHT GAIN -- GRAMS						
DOSE GROUP: DOSE LEVEL (MG/KG/DAY):		1 0	2 64	3 160	4 400	5 1000
day 1- 4 males	MEAN	3.3	3.3	3.1	3.1	2.6
	S.D.	0.57	0.46	0.81	0.79	1.04
	N	11	11	11	12	9
	females	MEAN	3.2	3.3	3.2	3.1
		S.D.	0.53	0.41	0.83	0.83
		N	11	11	12	12
	males+females	MEAN	3.2	3.3	3.2	3.1
day 4- 7 males		S.D.	0.53	0.42	0.86	0.81
		N	11	11	12	12
day 4-21 males	MEAN	6.5	6.4	6.1	6.1	4.9**
	S.D.	0.36	1.01	1.11	0.76	0.93
	N	11	11	11	12	9
	females	MEAN	6.2	6.1	6.0	6.0
		S.D.	0.41	0.83	1.03	0.70
		N	11	11	12	12
	males+females	MEAN	6.4	6.2	6.1	6.0
day 4-21 males		S.D.	0.36	0.91	1.05	0.72
		N	11	11	12	12
day 4-21 males	MEAN	44.1	43.2	42.3	44.0	39.4
	S.D.	3.06	4.29	5.89	5.25	4.76
	N	11	11	11	12	9
	females	MEAN	41.6	41.2	41.5	42.0
		S.D.	2.60	4.62	5.84	4.10
		N	11	11	12	12
	males+females	MEAN	42.8	42.2	42.3	43.0
day 4-21 males		S.D.	2.72	4.41	5.86	4.57
		N	11	11	12	12

Statistical key: ** = p<0.01

TABLE 17 - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

		SUMMARY OF PUP BODY WEIGHT GAIN -- GRAMS				
DOSE GROUP: DOSE LEVEL (MG/KG/DAY):		1 0	2 64	3 160	4 400	5 1000
day 7-14 males	MEAN	16.3	15.2	14.7	15.8	13.3**
	S.D.	1.65	2.13	1.98	1.57	1.97
	N	11	11	11	12	9
females	MEAN	15.6	14.7	14.9	15.2	13.7
	S.D.	1.33	1.93	2.22	1.60	2.09
	N	11	11	12	12	9
males+females	MEAN	15.9	15.0	15.0	15.5	13.5
	S.D.	1.42	2.00	2.25	1.55	2.29
	N	11	11	12	12	10
day 14-21 males	MEAN	21.3	21.6	21.5	22.1	21.1
	S.D.	2.52	2.42	3.65	3.64	2.31
	N	11	11	11	12	9
females	MEAN	19.8	20.4	20.6	20.8	20.9
	S.D.	1.84	2.65	3.38	2.50	3.23
	N	11	11	12	12	9
males+females	MEAN	20.5	21.0	21.2	21.5	21.2
	S.D.	2.11	2.49	3.39	2.98	2.70
	N	11	11	12	12	10

Statistical key: ** = p<0.01

	Summary of Clinical Observations F ₁ Treated Animals Preface	Table 18
--	---	----------

Number of animals examined represents the total number of animals observed.

Total represents a cumulative total of all animals with the indicated observation one or more times during the study.

Corresponding dose levels for each group were as follows:

Group I - 0 mg/kg/day
Group II - 64 mg/kg/day
Group III - 160 mg/kg/day
Group IV - 400 mg/kg/day
Group V - 1000 mg/kg/day

TABLE 18 - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

MALES

SUMMARY OF CLINICAL OBSERVATIONS

	DAY OF STUDY	
GROUP#	28	TOTAL

# OF ANIMALS EXAMINED	I	11
	II	11
	III	11
	IV	12
	V	10

Normal

WITHIN NORMAL LIMITS	I	11	11
	II	10	10
	III	11	11
	IV	12	12
	V	10	10

Dead

TERMINAL SACRIFICE	I	11	11
	II	11	11
	III	11	11
	IV	12	12
	V	10	10

Dermal-General

ALOPECIA - EXTREMITIES/SNOUT	I	0	0
	II	1	1
	III	0	0
	IV	0	0
	V	0	0

TABLE 18 - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

FEMALES

SUMMARY OF CLINICAL OBSERVATIONS

	DAY OF STUDY	
GROUP#	28	TOTAL

# OF ANIMALS EXAMINED	I	11
	II	11
	III	12
	IV	12
	V	10

Normal

WITHIN NORMAL LIMITS	I	11	11
	II	10	10
	III	12	12
	IV	12	12
	V	10	10

Dead

TERMINAL SACRIFICE	I	11	11
	II	11	11
	III	12	12
	IV	12	12
	V	10	10

Dermal-General

ALOPECIA -	I	0	0
EXTREMITIES/SNOUT	II	1	1
	III	0	0
	IV	0	0
	V	0	0

TABLE 19 - F1 TREATED ANIMALS
TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

MALES			MEAN BODY WEIGHT VALUES (GRAMS)				
			1	2	3	4	5
DOSE LEVEL (MG/KG/DAY):			0	64	160	400	1000
DAY 21	MEAN		54	55	53	54	47*
	S.D.		3.4	4.5	7.9	6.7	4.6
	N		11	11	11	12	10
DAY 24	MEAN		72	74	71	69	62**
	S.D.		3.7	4.9	9.1	7.4	7.4
	N		11	11	11	12	10
DAY 28	MEAN		99	101	99	99	87*
	S.D.		4.9	5.7	12.1	9.6	9.1
	N		11	11	11	12	10

Statistical key: * = p<0.05 . ** = p<0.01

FEMALES			MEAN BODY WEIGHT VALUES (GRAMS)				
			1	2	3	4	5
DOSE LEVEL (MG/KG/DAY):			0	64	160	400	1000
DAY 21	MEAN		52	52	50	53	49
	S.D.		3.6	6.5	8.6	7.2	7.3
	N		11	11	12	12	10
DAY 24	MEAN		68	68	64	66	62
	S.D.		4.2	8.0	9.8	7.3	7.2
	N		11	11	12	12	10
DAY 28	MEAN		91	91	87	89	84
	S.D.		5.3	10.3	11.5	9.3	6.5
	N		11	11	12	12	10

No statistically significant differences

MALES				MEAN BODY WEIGHT GAIN (GRAMS)				
DOSE GROUP:				1	2	3	4	5
DOSE LEVEL (MG/KG/DAY):				0	64	160	400	1000
DAY	21 TO	24	MEAN	18	18	18	15	15
			S.D.	1.0	1.8	1.7	2.7	5.1
			N	11	11	11	12	10
DAY	24 TO	28	MEAN	28	28	28	29	26
			S.D.	1.9	1.9	3.6	3.1	2.5
			N	11	11	11	12	10
DAY	21 TO	28	MEAN	45	46	45	45	40
			S.D.	2.5	2.5	5.1	4.4	6.8
			N	11	11	11	12	10

No statistically significant differences

TABLE 20 - F1 TREATED ANIMALS
TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

FEMALES				MEAN BODY WEIGHT GAIN (GRAMS)					
				DOSE GROUP:	1	2	3	4	5
				DOSE LEVEL (MG/KG/DAY) :	0	64	160	400	1000
DAY	21 TO	24	MEAN	15	16	14	13*	13	
			S.D.	1.2	2.4	2.0	2.2	2.6	
			N	11	11	12	12	10	
DAY	24 TO	28	MEAN	23	24	23	24	22	
			S.D.	1.6	2.7	3.1	3.0	1.8	
			N	11	11	12	12	10	
DAY	21 TO	28	MEAN	39	39	37	37	35	
			S.D.	2.5	4.9	4.4	4.1	3.7	
			N	11	11	12	12	10	

Statistical key: * = p<0.05

TABLE 21 - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENT TOXICITY SCREENING IN RATS

MEAN FEED CONSUMPTION VALUES (GRAMS/ANIMALS/DAY)

DOSE GROUP:			1	2	3	4	5
DOSE LEVEL (MG/KG/DAY):			0	64	160	400	1000
DAY	21 TO 24	MEAN	9.4	9.3	9.4	9.5	7.9
		S.D.	0.9	1.9	0.9	1.2	2.5
		N	10	10	10	12	5
DAY	24 TO 28	MEAN	13.2	13.8	13.4	14.0	12.8
		S.D.	1.1	1.1	1.4	1.0	0.9
		N	10	11	8	10	8
DAY	21 TO 28	MEAN	22.5	23.0	23.0	23.8	22.2
		S.D.	1.9	2.8	2.4	1.7	2.0
		N	9	10	7	10	3

Note: These means are approximations and should not be compared statistically, as they are derived from group-housed animals (in pairs and in threes)

	Incidence Summary Report for Gross Necropsy Observations – F ₀ Generation Preface	Table 22
--	--	----------

Corresponding dose levels for each group were as follows:

Group 1 - 0 mg/kg/day
Group 2 - 64 mg/kg/day
Group 3 - 160 mg/kg/day
Group 4 - 400 mg/kg/day
Group 5 - 1000 mg/kg/day

Incidence Summary Report for Gross Necropsy Observations
Study number: 034254

[illegible]

	Summary of Parental Organ Weights – F ₀ Generation Preface	Table 23
--	--	----------

Table of Contents

Summary of Absolute Organ Weights.....	89
Summary of Organ Weight to Body Weight Ratio.....	91

Huntingdon Life Sciences 03-4254

TABLE 23 - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

SUMMARY OF ABSOLUTE ORGAN WEIGHTS

MALES

DOSE GROUP: DOSE LEVEL (MG/KG/DAY):		1 0	2 64	3 160	4 400	5 1000
FINAL BODY WEIGHT g	MEAN	543	536	522	536	507
	S.D.	50.2	33.1	38.0	35.6	39.9
	N	12	12	12	12	12
TESTIS - RIGHT g	MEAN	1.7084	1.7779	1.7841	1.8066	1.8283
	S.D.	.14896	.15327	.13031	.10816	.09972
	N	12	12	12	12	12
TESTIS - LEFT g	MEAN	1.7013	1.7670	1.7834	1.8037	1.8402
	S.D.	.13294	.17810	.13222	.10997	.12217
	N	12	12	12	12	12
EPIDIDYMIS LEFT g	MEAN	0.6813	0.6978	0.7001	0.7048	0.6704
	S.D.	.04902	.05471	.03318	.03932	.04323
	N	12	12	12	12	12
EPIDIDYMIS RIGHT g	MEAN	0.6955	0.7724	0.7143	0.7036	0.6667
	S.D.	.05565	.24810	.04554	.03325	.04485
	N	12	12	12	12	12
KIDNEY LEFT g	MEAN	1.9591	2.0806	2.1443	2.2019*	2.3068**
	S.D.	.20419	.17400	.31377	.16484	.17379
	N	12	12	12	12	12
KIDNEY RIGHT g	MEAN	1.9745	2.0916	2.0853	2.2598**	2.3690**
	S.D.	.18138	.17360	.15111	.12365	.11334
	N	12	12	12	12	12
LIVER g	MEAN	21.033	20.776	20.297	20.508	22.661
	S.D.	3.1352	1.9378	2.1224	1.6009	2.2253
	N	12	12	12	12	12

Statistical key: * = p<0.05 ** = p<0.01

Huntingdon Life Sciences 03-4254

TABLE 23 - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

SUMMARY OF ABSOLUTE ORGAN WEIGHTS

FEMALES

DOSE GROUP:		1	2	3	4	5
DOSE LEVEL (MG/KG/DAY):		0	64	160	400	1000
FINAL BODY WEIGHT g	MEAN	332	333	326	334	346
	S.D.	18.2	30.9	26.8	25.1	24.2
	N	11	11	12	12	10
KIDNEY LEFT g	MEAN	1.4209	1.4009	1.4168	1.4572	1.4780
	S.D.	.12379	.13006	.16407	.16343	.18486
	N	11	11	12	12	10
KIDNEY RIGHT g	MEAN	1.4096	1.4395	1.4184	1.4634	1.5109
	S.D.	.11311	.12786	.18231	.14670	.17642
	N	11	11	12	12	10
LIVER g	MEAN	18.105	17.390	16.874	18.400	19.513
	S.D.	2.0242	1.9527	2.5130	2.2115	2.7759
	N	11	11	12	12	10

No statistically significant differences

Huntingdon Life Sciences 03-4254

TABLE 23 - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

SUMMARY OF ORGAN WEIGHT TO BODY WEIGHT RATIO

MALES

DOSE GROUP: DOSE LEVEL (MG/KG/DAY):		1 0	2 64	3 160	4 400	5 1000
FINAL BODY WEIGHT g	MEAN	543	536	522	536	507
	S.D.	50.2	33.1	38.0	35.6	39.9
	N	12	12	12	12	12
TESTIS - RIGHT Ratio	MEAN	0.0032	0.0033	0.0034	0.0034	0.0036**
	S.D.	.00034	.00031	.00041	.00028	.00036
	N	12	12	12	12	12
TESTIS - LEFT Ratio	MEAN	0.0032	0.0033	0.0034	0.0034	0.0037**
	S.D.	.00030	.00033	.00038	.00026	.00037
	N	12	12	12	12	12
EPIDIDYMIS LEFT Ratio	MEAN	0.0013	0.0013	0.0013	0.0013	0.0013
	S.D.	.00013	.00010	.00010	.00011	.00012
	N	12	12	12	12	12
EPIDIDYMIS RIGHT Ratio	MEAN	0.0013	0.0014	0.0014	0.0013	0.0013
	S.D.	.00014	.00044	.00014	.00011	.00013
	N	12	12	12	12	12
KIDNEY LEFT Ratio	MEAN	0.0036	0.0039	0.0041*	0.0041*	0.0046**
	S.D.	.00025	.00031	.00069	.00028	.00033
	N	12	12	12	12	12
KIDNEY RIGHT Ratio	MEAN	0.0036	0.0039	0.0040**	0.0042**	0.0047**
	S.D.	.00024	.00030	.00017	.00032	.00029
	N	12	12	12	12	12
LIVER Ratio	MEAN	0.0386	0.0387	0.0389	0.0383	0.0448**
	S.D.	.00296	.00228	.00245	.00256	.00358
	N	12	12	12	12	12

Statistical key: * = p<0.05 ** = p<0.01

Huntingdon Life Sciences 03-4254

TABLE 23 - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

SUMMARY OF ORGAN WEIGHT TO BODY WEIGHT RATIO

FEMALES

DOSE GROUP:		1	2	3	4	5
DOSE LEVEL (MG/KG/DAY):		0	64	160	400	1000
FINAL BODY WEIGHT g	MEAN	332	333	326	334	346
	S.D.	18.2	30.9	26.8	25.1	24.2
	N	11	11	12	12	10
KIDNEY LEFT Ratio	MEAN	0.0043	0.0042	0.0043	0.0044	0.0043
	S.D.	.00030	.00026	.00035	.00032	.00037
	N	11	11	12	12	10
KIDNEY RIGHT Ratio	MEAN	0.0043	0.0043	0.0043	0.0044	0.0044
	S.D.	.00041	.00018	.00042	.00030	.00040
	N	11	11	12	12	10
LIVER Ratio	MEAN	0.0545	0.0521	0.0516	0.0549	0.0563
	S.D.	.00483	.00286	.00550	.00432	.00605
	N	11	11	12	12	10

No statistically significant differences

	Lesion Incidence Summary with Expanded Severity Levels – F ₀ Generation Preface	Table 24
--	--	----------

Corresponding dose levels for each group were as follows:

Group 1 - 0 mg/kg/day
Group 2 - 64 mg/kg/day
Group 3 - 160 mg/kg/day
Group 4 - 400 mg/kg/day
Group 5 - 1000 mg/kg/day

Key to Abbreviations

Ctls = Controls (Group 1)
Fallop = Fallopian tubes
NAD = No abnormal diagnoses

TBA
Reproduction/Developmental Toxicity Screening Test in Rats

Incidence Summary of Microscopic Findings with Severity Levels
All Animals

		-- A n i m a l s --		A f f e c t e d . --	
Controls from group(s): 1		-- M a l e s --		-- F e m a l e s --	
		Ctl's		Ctl's	
T i s s u e s W i t h D i a g n o s e s	No. in group:	12	12	12	12
Left Epididymis	Number examined:	12	12		
Left Testis	Number examined:	12	12		
TUBULAR DEGENERATION/ATROPHY					
	Nad>	12	11		
	Slight>	0	1		
.....	Total Incidence of Finding Observed:	0	1		
Ovaries	Number examined:			12	12
Oviducts/Fallop	Number examined:			12	12
Parathyroid	Number examined:	12	12	12	11
Thyroid	Number examined:	12	12	12	12
ECTOPIC THYMIC TISSUE					
	Nad>	11	12	12	12
	Present>	1	0	0	0
.....	Total Incidence of Finding Observed:	1	0	0	0

All Diagnoses; Phases: All; Death types: All scheduled; Date of death range: 11-Aug-03 To 03-Sep-03

Huntingdon Life Sciences 03-4254

TABLE 25 - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

		SUMMARY OF PUP NECROPSY OBSERVATIONS				
		1	2	3	4	5
DOSE LEVEL (MG/KG/DAY):		0	64	160	400	1000
Litters Evaluated	N	11	11	12	12	11
Pups Evaluated	N	147	132	145	149	119
Live	N	144	131	143	145	113
Stillborn	N	3	1	2	4	6
GROSS EXAM						

Litter Incidence	N	0	0	3	0	5
Pup Incidence	N	0	0	5	0	11
AUTOLYSIS						
Pup Incidence	N	0	0	1	0	7
	%	0.0	0.0	0.7	0.0	5.9
Litter Incidence	N	0	0	1	0	5
	%	0.0	0.0	8.3	0.0	45.5
CANNIBALIZED						
Pup Incidence	N	0	0	4	0	4
	%	0.0	0.0	2.8	0.0	3.4
Litter Incidence	N	0	0	2	0	2
	%	0.0	0.0	16.7	0.0	18.2
LUNGS						

Litter Incidence	N	5	1	1	2	5
Pup Incidence	N	5	3	2	4	18
FLOATATION TEST - STILLBORN						
Pup Incidence	N	3	1	0	4	0
	%	2.0	0.8	0.0	2.7	0.0
Litter Incidence	N	3	1	0	2	0
	%	27.3	9.1	0.0	16.7	0.0
FLOATATION TEST - FOUND DEAD						
Pup Incidence	N	2	1	1	0	18
	%	1.4	0.8	0.7	0.0	15.1
Litter Incidence	N	2	1	1	0	5
	%	18.2	9.1	8.3	0.0	45.5

Huntingdon Life Sciences 03-4254

TABLE 25 - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

		SUMMARY OF PUP NECROPSY OBSERVATIONS				
DOSE GROUP:		1	2	3	4	5
DOSE LEVEL (MG/KG/DAY):		0	64	160	400	1000
Litters Evaluated	N	11	11	12	12	11
Pups Evaluated	N	147	132	145	149	119
Live	N	144	131	141	145	113
Stillborn	N	3	1	4	4	6
GROSS EXAM						

Litter Incidence	N	0	0	3	0	5
Pup Incidence	N	0	0	5	0	11
AUTOLYSIS						
Pup Incidence	N	0	0	1	0	7
	%	0.0	0.0	0.7	0.0	5.9
Litter Incidence	N	0	0	1	0	5
	%	0.0	0.0	8.3	0.0	45.5
CANNIBALIZED						
Pup Incidence	N	0	0	4	0	4
	%	0.0	0.0	2.8	0.0	3.4
Litter Incidence	N	0	0	2	0	2
	%	0.0	0.0	16.7	0.0	18.2
LUNGS						

Litter Incidence	N	5	1	1	2	5
Pup Incidence	N	5	3	2	4	18
FLOATATION TEST - STILLBORN						
Pup Incidence	N	3	1	0	4	0
	%	2.0	0.8	0.0	2.7	0.0
Litter Incidence	N	3	1	0	2	0
	%	27.3	9.1	0.0	16.7	0.0
FLOATATION TEST - FOUND DEAD						
Pup Incidence	N	2	1	1	0	18
	%	1.4	0.8	0.7	0.0	15.1
Litter Incidence	N	2	1	1	0	5
	%	18.2	9.1	8.3	0.0	45.5

Huntingdon Life Sciences 03-4254

TABLE 25 - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

		SUMMARY OF PUP NECROPSY OBSERVATIONS				
		1	2	3	4	5
DOSE LEVEL (MG/KG/DAY):		0	64	160	400	1000
Litters Evaluated	N	11	11	12	12	11
Pups Evaluated	N	147	132	145	149	119
Live	N	144	131	141	145	113
Stillborn	N	3	1	4	4	6
DISCOLORED FOCI						
Pup Incidence	N	0	0	1	0	0
	%	0.0	0.0	0.7	0.0	0.0
Litter Incidence	N	0	0	1	0	0
	%	0.0	0.0	8.3	0.0	0.0
FLUID-FILLED						
Pup Incidence	N	0	1	0	0	0
	%	0.0	0.8	0.0	0.0	0.0
Litter Incidence	N	0	1	0	0	0
	%	0.0	9.1	0.0	0.0	0.0
STOMACH						
Litter Incidence	N	10	5	6	6	6
Pup Incidence	N	22	7	16	10	20
NO MILK IN STOMACH						
Pup Incidence	N	21	5	15	9	18
	%	14.3	3.8	10.3	6.0	15.1
Litter Incidence	N	10	4	5	5	6
	%	90.9	36.4	41.7	41.7	54.5
MILK IN STOMACH						
Pup Incidence	N	1	2	1	1	2
	%	0.7	1.5	0.7	0.7	1.7
Litter Incidence	N	1	2	1	1	2
	%	9.1	18.2	8.3	8.3	18.2

Huntingdon Life Sciences 03-4254

TABLE 25 - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

SUMMARY OF PUP NECROPSY OBSERVATIONS						
DOSE GROUP:		1	2	3	4	5
DOSE LEVEL (MG/KG/DAY):		0	64	160	400	1000
Litters Evaluated	N	11	11	12	12	11
Pups Evaluated	N	147	132	145	149	119
Live	N	144	131	141	145	113
Stillborn	N	3	1	4	4	6
KIDNEY						

Litter Incidence	N	0	1	0	0	0
Pup Incidence	N	0	1	0	0	0
V DILATED RENAL PELVIS (PAPILLA REDUCED)						
Pup Incidence	N	0	1	0	0	0
	%	0.0	0.8	0.0	0.0	0.0
Litter Incidence	N	0	1	0	0	0
	%	0.0	9.1	0.0	0.0	0.0
GONADS						

Litter Incidence	N	0	0	1	0	1
Pup Incidence	N	0	0	1	0	1
M UNDESCENDED TESTE(S)						
Pup Incidence	N	0	0	1	0	1
	%	0.0	0.0	0.7	0.0	0.8
Litter Incidence	N	0	0	1	0	1
	%	0.0	0.0	8.3	0.0	9.1
SKIN						

Litter Incidence	N	0	0	0	0	1
Pup Incidence	N	0	0	0	0	1
SCAB						
Pup Incidence	N	0	0	0	0	1
	%	0.0	0.0	0.0	0.0	0.8
Litter Incidence	N	0	0	0	0	1
	%	0.0	0.0	0.0	0.0	9.1

Huntingdon Life Sciences 03-4254

TABLE 25 - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

SUMMARY OF PUP NECROPSY OBSERVATIONS						
DOSE GROUP:		1	2	3	4	5
DOSE LEVEL (MG/KG/DAY):		0	64	160	400	1000
Litters Evaluated	N	11	11	12	12	11
Pups Evaluated	N	147	132	145	149	119
Live	N	144	131	141	145	113
Stillborn	N	3	1	4	4	6
THORACIC CAVITY						
Litter Incidence	N	0	1	0	0	0
Pup Incidence	N	0	1	0	0	0
MASS						
Pup Incidence	N	0	1	0	0	0
	%	0.0	0.8	0.0	0.0	0.0
Litter Incidence	N	0	1	0	0	0
	%	0.0	9.1	0.0	0.0	0.0

TABLE 26 - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

SUMMARY OF PARENTAL NECROPSY OBSERVATIONS

DOSE GROUP:		1	2	3	4	5
DOSE LEVEL (MG/KG/DAY):		0	64	160	400	1000
MALES	N	11	11	11	12	10
KIDNEY	N	1	0	0	0	0

DILATED RENAL PELVIS	N	1	0	0	0	0
	%	9.1	0.0	0.0	0.0	0.0
ENLARGED KIDNEY	N	1	0	0	0	0
	%	9.1	0.0	0.0	0.0	0.0
SMALL KIDNEY	N	1	0	0	0	0
	%	9.1	0.0	0.0	0.0	0.0

TABLE 26 - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

SUMMARY OF PARENTAL NECROPSY OBSERVATIONS

DOSE GROUP: DOSE LEVEL (MG/KG/DAY):		1 0	2 64	3 160	4 400	5 1000
FEMALES	N	11	11	12	12	10
KIDNEY	N	0	2	0	0	1

DILATED RENAL PELVIS	N	0	1	0	0	1
	%	0.0	9.1	0.0	0.0	10.0
CYSTIC KIDNEY	N	0	1	0	0	0
	%	0.0	9.1	0.0	0.0	0.0

	Analytical Report	Appendix A
--	-------------------	------------

STUDY TITLE**Analytical Report For:****TBA: Reproduction/Developmental Toxicity Screening Test in Rats****AUTHOR****Cindy Rao****REPORT DATE****4 February 2004****STUDY NUMBER****03-4254**

	Analytical Report	Appendix A
--	-------------------	------------

Signatures

Written by:



Cindy Rao
Scientist II
Formulation Chemistry Services

05 Feb 04

Date

Reviewed by:

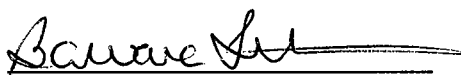


Kay Saladdin
Associate Director
Formulation Chemistry Services

05 Feb 04

Date

Approved by:



Barbara L. Litzenberger
Director
Analytical Services

05 Feb 04

Date

	Analytical Report	Appendix A
--	-------------------	------------

Table of Contents

Study Title Page.....	102
Signatures.....	103
Table of Contents.....	104
1. Summary.....	105
2. Experimental Procedures.....	105
3. Results and Discussion.....	106

Tables

Table I: Summary of Stability of TBA in Water	107
Table I-A: Results of Day 0 Stability (Room Temperature)	107
Table I-B: Results of Day 8 Stability (Room Temperature)	107
Table II: Summary of Dose Confirmation of TBA	108
Table II-A: Results of Dose Confirmation 1 (Week 1).....	108
Table II-B: Results of Dose Confirmation 2 (Week 5).....	109
Table II-C: Results of Dose Confirmation 3 (Week 12)	110

Figures

Figure I: Typical Gas Chromatogram of Group 1 (0.0 mg/mL)	111
Figure II: Typical Gas Chromatogram of Group 2 (12.8 mg/mL)	112
Figure III: Typical Gas Chromatogram of Group 3 (32.0 mg/mL)	113
Figure IV: Typical Gas Chromatogram of Group 4 (80.0 mg/mL).....	114
Figure V: Typical Gas Chromatogram of Group 5 (200.0 mg/mL).....	115

	Analytical Report	Appendix A
--	-------------------	------------

1. Summary

Dose solutions of the test article, Tertiary Butanol (TBA) in water were analyzed to confirm that the prepared dose solutions were stable for 8 days when stored at room temperature, and that the administered TBA concentrations were appropriate under the study conditions.

The analytical method validated at Huntingdon Life Sciences (HLS-009-03) involved the dilution of TBA with methanol, followed by quantification of the compound using Gas Chromatography-FID detection (Hewlett Packard, GC-FID).

2. Experimental Procedures

2.1 The analytical method (HLS-009-03) was validated by Formulation Chemistry Services at HLS. Details of the analytical method and method validation are maintained in the study files for Study No. 03-4254.

2.2 TBA Solution received from Pharmacy at HLS were diluted with methanol and analyzed using a Gas Chromatograph equipped with a HP Plot Q (30 m × 0.32 mm, 20 µm film thickness) column and a FID detection. PE Nelson Turbochrom installed on a personal computer was used for data collection and processing. The limit of quantification (LOQ) of the test article was determined as 200.00 mcg/mL and the quantification was based on the calibration range of approximately 200.00 -1000.00 mcg/mL.

2.3 Date of Sample Receipt and Analysis:

Interval	Date of Mix Preparation	Date Received	Date Analyzed
Day 0 Stability (Room Temperature)	09 Jun 03	09 Jun 03	09 Jun 03
Day 8 Stability (Room Temperature)	09 Jun 03	17 Jun 03	17 Jun 03
Dose Confirmation (Week 1)	16 Jun 03	17 Jun 03	17 Jun 03
Dose Confirmation (Week 5)	14 Jul 03	15 Jul 03	15-16 Jul 03
Dose Confirmation (Week 12)	01 Sep 03	02 Sep 03	02 Sep 03

	Analytical Report	Appendix A
--	-------------------	------------

3. Results and Discussion

- 3.1 Stability: Stability was determined for the low and high dose levels. The preliminary mixes of TBA in water proved to be stable for 8 days when stored at room temperature and the mean % nominal values of all samples were within $\pm 10\%$ of initial concentrations (Day 0) (see Table I, I-A and I-B).
- 3.2 Dose Confirmation: All groups were assayed in duplicate for weeks 1, 5 & 12. The % nominal values (See Table II, II-A, II-B and II-C) for all dose groups were within HLS's SOP specified limits. The concentrations of duplicate of the samples were within $\pm 10\%$ of each other, and the means of concentration were within $\pm 10\%$ of nominal.

	Analytical Report	Appendix A
--	-------------------	------------

Table I: Summary of Stability of TBA in Water

(as Mean % Nominal Concentration)

Interval	Group 2 ^a	Group 5 ^a
Stability (Day 0)	94.1	97.5
Stability (Day 8)	93.7	98.1

^a Average of duplicate measurements.**Table I-A: Results of Day 0 Stability (Room Temperature)**

Sample ID	Total mcg/mL Found	mcg/mL Added	% Nominal ^b	Mean % Nominal
LQC 1 ^a	4578.81	5000.00	91.6	-
LQC 2 ^a	4503.69	5000.00	90.1	
HQC 1 ^a	197801.40	200000.00	98.9	
HQC 2 ^a	198882.08	200000.00	99.4	
Group 2 A	12193.04	12800.00	95.3	94.1
Group 2 B	11882.08	12800.00	92.8	
Group 5 A	195576.93	200000.00	97.8	97.5
Group 5 B	194269.50	200000.00	97.1	

^a LQC = Low quality control, HQC = High quality control.^b % Nominal = (Total mcg/mL Found / mcg/mL Added) x100%.

- = Non-calculable.

Table I-B: Results of Day 8 Stability (Room Temperature)

Sample ID	Total mcg/mL Found	mcg/mL Added	% Nominal ^b	Mean % Nominal
LQC 1 ^a	4655.13	5000.00	93.1	-
LQC 2 ^a	4688.56	5000.00	93.8	
HQC 1 ^a	202428.48	200000.00	101.2	
HQC 2 ^a	206018.56	200000.00	103.0	
Group 2 A	12115.82	12800.00	94.7	93.7
Group 2 B	11869.35	12800.00	92.7	
Group 5 A	195914.07	200000.00	98.0	98.1
Group 5 B	196363.77	200000.00	98.2	

^a LQC = Low quality control, HQC = High quality control.^b % Nominal = (Total mcg/mL Found / mcg/mL Added) x100%.

- = Non-calculable.

	Analytical Report	Appendix A
--	-------------------	------------

Table II: Summary of Dose Confirmation of TBA

(as Mean % Nominal Concentration)

Interval	Group 1 ^a	Group 2 ^a	Group 3 ^a	Group 4 ^a	Group 5 ^a
Week 1	ND ^b	95.6	98.2	101.8	98.4
Week 5	ND ^b	96.3	91.6	91.7	104.3
Week 12	ND ^b	98.9	96.7	101.1	97.7

^a Average of duplicate measurements.^b None detected.**Table II-A: Results of Dose Confirmation 1 (Week 1)**

Sample ID	Total mcg/mL Found	mcg/mL Added	% Nominal ^c	Mean % Nominal
LQC 1 ^a	4655.13	5000.00	93.1	-
LQC 2 ^a	4688.56	5000.00	93.8	
HQC 1 ^a	202428.48	200000.00	101.2	
HQC 2 ^a	206018.56	200000.00	103.0	
Group 1 A	ND ^b	0.00	-	-
Group 1 B	ND ^b	0.00	-	
Group 2 A	12592.34	12800.00	98.4	95.6
Group 2 B	11869.08	12800.00	92.7	
Group 3 A	31232.10	32000.00	97.6	98.2
Group 3 B	31631.44	32000.00	98.8	
Group 4 A	81964.91	80000.00	102.5	101.8
Group 4 B	80830.04	80000.00	101.0	
Group 5 A	197044.21	200000.00	98.5	98.4
Group 5 B	196535.65	200000.00	98.3	

^a LQC = Low quality control, HQC = High quality control.^b ND = None Detected.^c % Nominal = (Total mcg/mL Found / mcg/mL Added) x100%.

- = Non-calculable.

	Analytical Report	Appendix A
--	-------------------	------------

Table II-B: Results of Dose Confirmation 2 (Week 5)

Sample ID	Total mcg/mL Found	mcg/mL Added	% Nominal ^c	Mean % Nominal
LQC 1 ^a	5389.20	5000.00	107.8	-
LQC 2 ^a	5400.49	5000.00	108.0	
HQC 1 ^a	214590.46	200000.00	107.3	
HQC 2 ^a	208248.19	200000.00	104.1	
Group 1 A	ND ^b	0.00	-	-
Group 1 B	ND ^b	0.00	-	
Group 2 A	11899.22	12800.00	93.0	96.3
Group 2 B	12730.22	12800.00	99.5	
Group 3 A	29173.22	32000.00	91.2	91.6
Group 3 B	29446.80	32000.00	92.0	
Group 4 A	73023.42	80000.00	91.3	91.7
Group 4 B	73715.88	80000.00	92.1	
Group 5 A	206262.00	200000.00	103.1	104.3
Group 5 B	210745.25	200000.00	105.4	

^a LQC = Low quality control, HQC = High quality control.^b ND = None Detected.^c % Nominal = (Total mcg/mL Found / mcg/mL Added) x100%.

- = Non-calculable.

	Analytical Report	Appendix A
--	-------------------	------------

Table II-C: Results of Dose Confirmation 3 (Week 12)

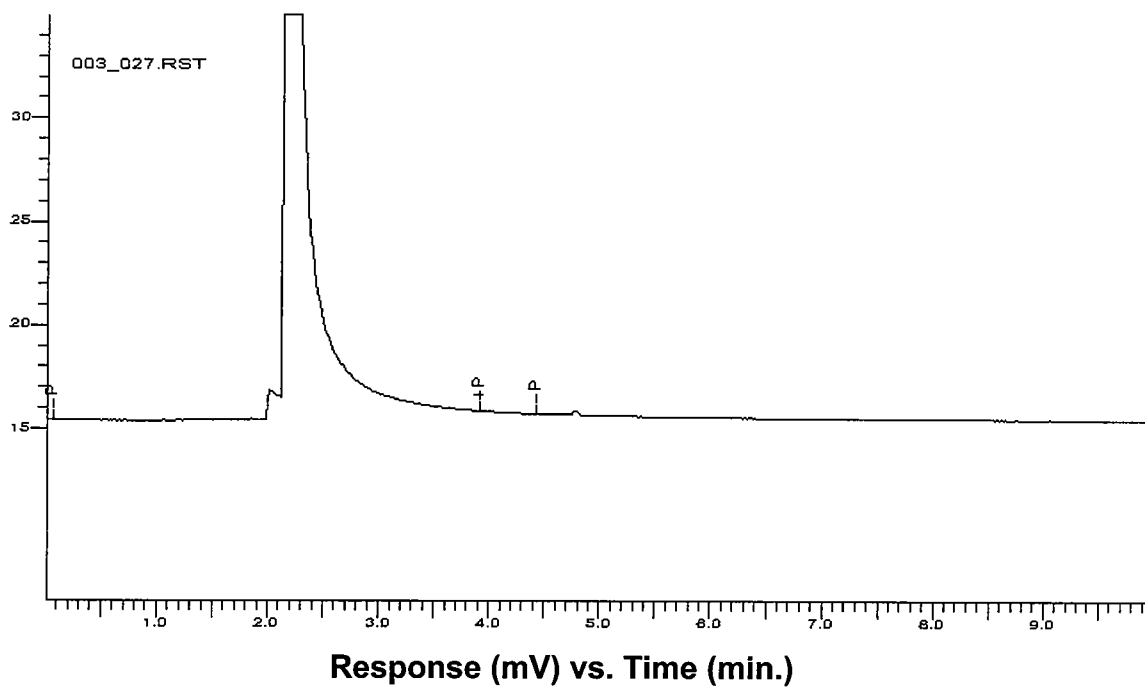
Sample ID	Total mcg/mL Found	mcg/mL Added	% Nominal ^c	Mean % Nominal
LQC 1 ^a	4722.39	5000.00	94.4	-
LQC 2 ^a	5373.80	5000.00	107.5	
HQC 1 ^a	199974.13	200000.00	100.0	
HQC 2 ^a	210582.86	200000.00	105.3	
Group 1 A	ND ^b	0.00	-	-
Group 1 B	ND ^b	0.00	-	
Group 2 A	12781.08	12800.00	99.9	98.9
Group 2 B	12530.84	12800.00	97.9	
Group 3 A	30954.43	32000.00	96.7	96.7
Group 3 B	30928.22	32000.00	96.7	
Group 4 A	80377.29	80000.00	100.5	101.1
Group 4 B	81273.27	80000.00	101.6	
Group 5 A	195652.56	200000.00	97.8	97.7
Group 5 B	195277.08	200000.00	97.6	

^a LQC = Low quality control, HQC = High quality control.^b ND = None Detected.^c % Nominal = (Total mcg/mL Found / mcg/mL Added) x100%.

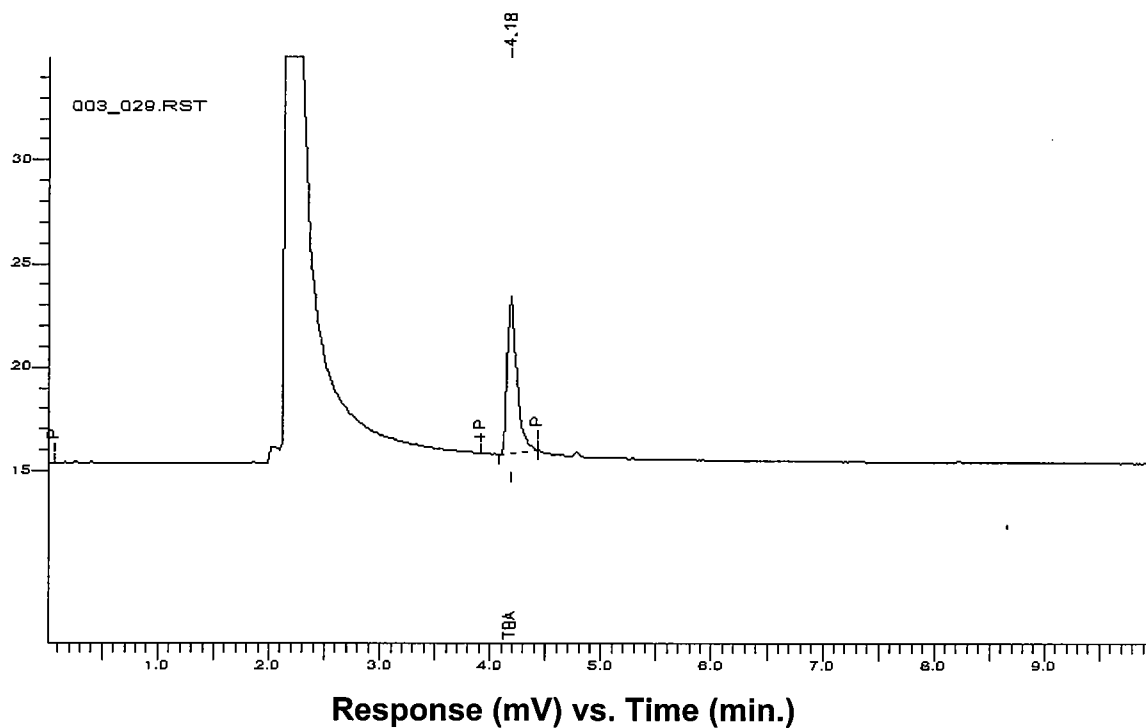
- = Non-calculable.

	Analytical Report	Appendix A
--	-------------------	------------

Figure I: Typical Gas Chromatogram of Group 1 (0.0 mg/mL)

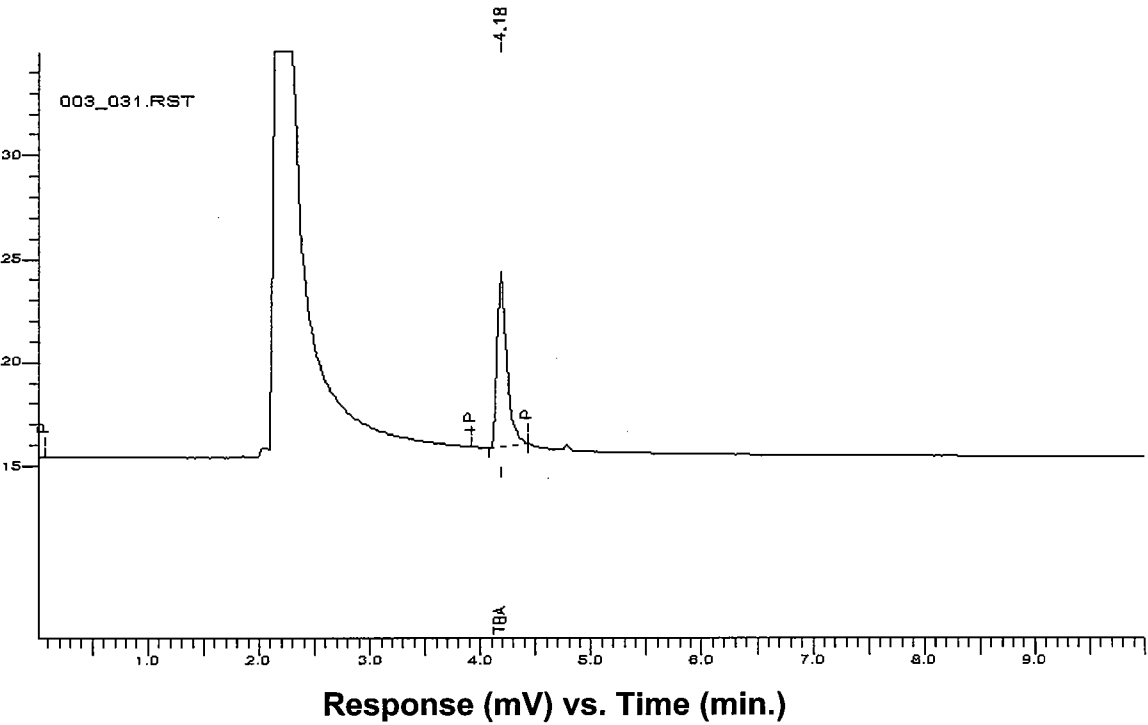


	Analytical Report	Appendix A
--	-------------------	------------

Figure II: Typical Gas Chromatogram of Group 2 (12.8 mg/mL)

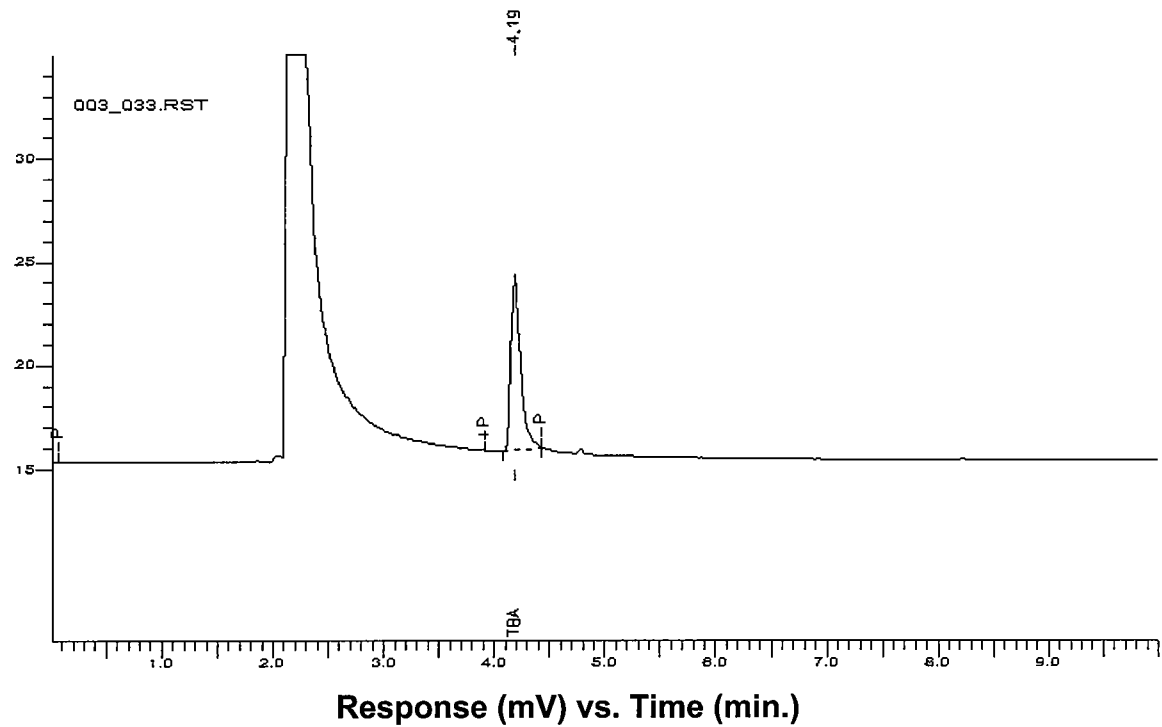
	Analytical Report	Appendix A
--	-------------------	------------

Figure III: Typical Gas Chromatogram of Group 3 (32.0 mg/mL)



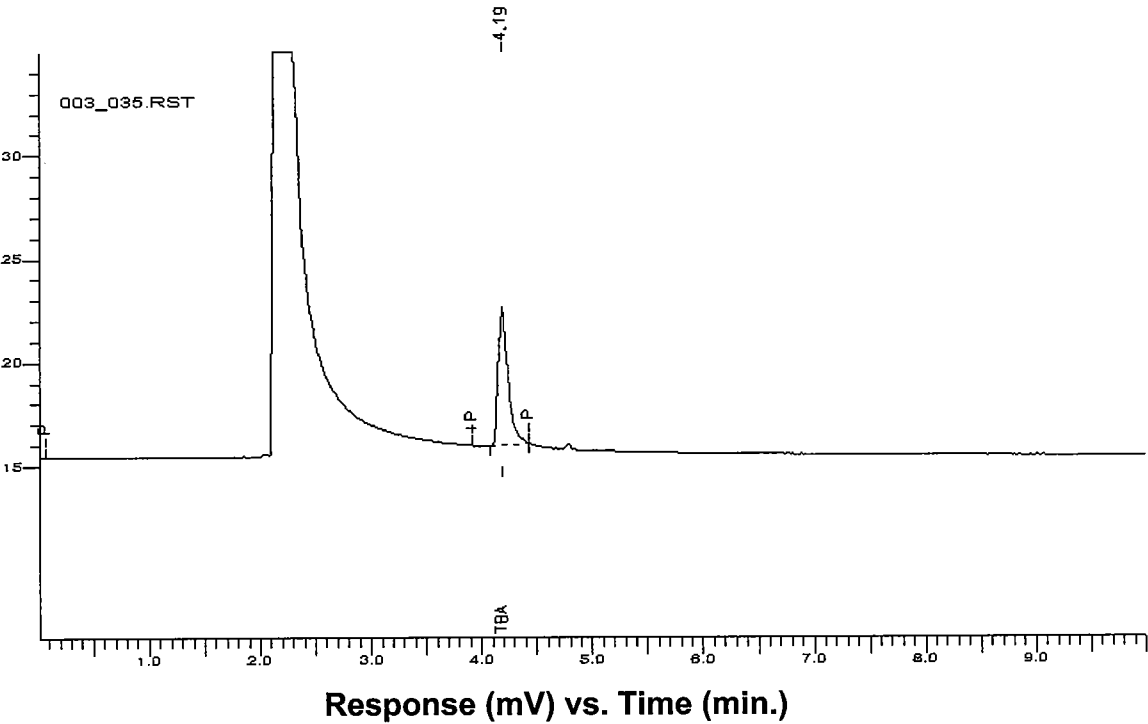
	Analytical Report	Appendix A
--	-------------------	------------

Figure IV: Typical Gas Chromatogram of Group 4 (80.0 mg/mL)



	Analytical Report	Appendix A
--	-------------------	------------

Figure V: Typical Gas Chromatogram of Group 5 (200.0 mg/mL)



5-FEB-2004 17:22

Huntingdon Life Sciences 03-4254

PAGE 116

APPENDIX B - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

MALES GROUP 1 0 MG/KG/DAY INDIVIDUAL ANIMAL TERMINATION HISTORY

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY
1063	TERMINAL SACRIFICE	20-AUG-03	64
1064	TERMINAL SACRIFICE	20-AUG-03	64
1065	TERMINAL SACRIFICE	20-AUG-03	64
1066	TERMINAL SACRIFICE	20-AUG-03	64
1067	TERMINAL SACRIFICE	20-AUG-03	64
1068	TERMINAL SACRIFICE	20-AUG-03	64
1069	TERMINAL SACRIFICE	20-AUG-03	64
1070	TERMINAL SACRIFICE	20-AUG-03	64
1071	TERMINAL SACRIFICE	20-AUG-03	64
1072	TERMINAL SACRIFICE	20-AUG-03	64
1073	TERMINAL SACRIFICE	20-AUG-03	64
1074	TERMINAL SACRIFICE	20-AUG-03	64

5-FEB-2004 17:22

Huntingdon Life Sciences 03-4254

PAGE 117

APPENDIX B - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

MALES GROUP 2 64 MG/KG/DAY INDIVIDUAL ANIMAL TERMINATION HISTORY

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY
2063	TERMINAL SACRIFICE	20-AUG-03	64
2064	TERMINAL SACRIFICE	20-AUG-03	64
2065	TERMINAL SACRIFICE	20-AUG-03	64
2066	TERMINAL SACRIFICE	20-AUG-03	64
2067	TERMINAL SACRIFICE	20-AUG-03	64
2068	TERMINAL SACRIFICE	20-AUG-03	64
2069	TERMINAL SACRIFICE	20-AUG-03	64
2070	TERMINAL SACRIFICE	20-AUG-03	64
2071	TERMINAL SACRIFICE	20-AUG-03	64
2072	TERMINAL SACRIFICE	20-AUG-03	64
2073	TERMINAL SACRIFICE	20-AUG-03	64
2074	TERMINAL SACRIFICE	20-AUG-03	64

5-FEB-2004 17:22

Huntingdon Life Sciences 03-4254

PAGE 118

APPENDIX B - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL ANIMAL TERMINATION HISTORY

MALES GROUP 3 160 MG/KG/DAY

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY
3063	TERMINAL SACRIFICE	20-AUG-03	64
3064	TERMINAL SACRIFICE	20-AUG-03	64
3065	TERMINAL SACRIFICE	20-AUG-03	64
3066	TERMINAL SACRIFICE	20-AUG-03	64
3067	TERMINAL SACRIFICE	20-AUG-03	64
3068	TERMINAL SACRIFICE	20-AUG-03	64
3069	TERMINAL SACRIFICE	20-AUG-03	64
3070	TERMINAL SACRIFICE	20-AUG-03	64
3071	TERMINAL SACRIFICE	20-AUG-03	64
3072	TERMINAL SACRIFICE	20-AUG-03	64
3073	TERMINAL SACRIFICE	20-AUG-03	64
3074	TERMINAL SACRIFICE	20-AUG-03	64

5-FEB-2004 17:22

Huntingdon Life Sciences 03-4254

PAGE 119

APPENDIX B - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL ANIMAL TERMINATION HISTORY

MALES GROUP 4 400 MG/KG/DAY

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY
4063	TERMINAL SACRIFICE	20-AUG-03	64
4064	TERMINAL SACRIFICE	20-AUG-03	64
4065	TERMINAL SACRIFICE	20-AUG-03	64
4066	TERMINAL SACRIFICE	20-AUG-03	64
4067	TERMINAL SACRIFICE	20-AUG-03	64
4068	TERMINAL SACRIFICE	20-AUG-03	64
4069	TERMINAL SACRIFICE	20-AUG-03	64
4070	TERMINAL SACRIFICE	20-AUG-03	64
4071	TERMINAL SACRIFICE	20-AUG-03	64
4072	TERMINAL SACRIFICE	20-AUG-03	64
4073	TERMINAL SACRIFICE	20-AUG-03	64
4074	TERMINAL SACRIFICE	20-AUG-03	64

5-FEB-2004 17:22

Huntingdon Life Sciences 03-4254

PAGE 120

APPENDIX B - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL ANIMAL TERMINATION HISTORY

MALES GROUP 5 1000 MG/KG/DAY

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY
5063	TERMINAL SACRIFICE	20-AUG-03	64
5064	TERMINAL SACRIFICE	20-AUG-03	64
5065	TERMINAL SACRIFICE	20-AUG-03	64
5066	TERMINAL SACRIFICE	20-AUG-03	64
5067	TERMINAL SACRIFICE	20-AUG-03	64
5068	TERMINAL SACRIFICE	20-AUG-03	64
5069	TERMINAL SACRIFICE	20-AUG-03	64
5070	TERMINAL SACRIFICE	20-AUG-03	64
5071	TERMINAL SACRIFICE	20-AUG-03	64
5072	TERMINAL SACRIFICE	20-AUG-03	64
5073	TERMINAL SACRIFICE	20-AUG-03	64
5074	TERMINAL SACRIFICE	20-AUG-03	64

APPENDIX B - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL ANIMAL TERMINATION HISTORY

FEMALES GROUP 1 0 MG/KG/DAY

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY	PREGNANCY STATUS
1563	TERMINAL SACRIFICE	28-AUG-03	72	P
1564	TERMINAL SACRIFICE	3-SEP-03	78	P
1565	TERMINAL SACRIFICE	28-AUG-03	72	P
1566	TERMINAL SACRIFICE	30-AUG-03	74	P
1567	TERMINAL SACRIFICE	11-AUG-03	55	NP
1568	TERMINAL SACRIFICE	28-AUG-03	72	P
1569	TERMINAL SACRIFICE	29-AUG-03	73	P
1570	TERMINAL SACRIFICE	28-AUG-03	72	P
1571	TERMINAL SACRIFICE	30-AUG-03	74	P
1572	TERMINAL SACRIFICE	31-AUG-03	75	P
1573	TERMINAL SACRIFICE	28-AUG-03	72	P
1574	TERMINAL SACRIFICE	30-AUG-03	74	P

NP-NOT PREGNANT, P-PREGNANT

5-FEB-2004 17:22

Huntingdon Life Sciences 03-4254

PAGE 122

APPENDIX B - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL ANIMAL TERMINATION HISTORY

FEMALES GROUP 2 64 MG/KG/DAY

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY	PREGNANCY STATUS
2563	TERMINAL SACRIFICE	29-AUG-03	73	P
2564	TERMINAL SACRIFICE	2-SEP-03	77	P
2565	TERMINAL SACRIFICE	28-AUG-03	72	P
2566	TERMINAL SACRIFICE	27-AUG-03	71	P
2567	TERMINAL SACRIFICE	31-AUG-03	75	P
2568	TERMINAL SACRIFICE	31-AUG-03	75	P
2569	TERMINAL SACRIFICE	30-AUG-03	74	P
2570	TERMINAL SACRIFICE	27-AUG-03	71	P
2571	TERMINAL SACRIFICE	31-AUG-03	75	P
2572	TERMINAL SACRIFICE	12-AUG-03	56	NP
2573	TERMINAL SACRIFICE	29-AUG-03	73	P
2574	TERMINAL SACRIFICE	30-AUG-03	74	P

NP-NOT PREGNANT, P-PREGNANT

5-FEB-2004 17:22

Huntingdon Life Sciences 03-4254

PAGE 123

APPENDIX B - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL ANIMAL TERMINATION HISTORY

FEMALES GROUP 3 160 MG/KG/DAY

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY	PREGNANCY STATUS
3563	TERMINAL SACRIFICE	29-AUG-03	73	P
3564	TERMINAL SACRIFICE	28-AUG-03	72	P
3565	TERMINAL SACRIFICE	5-SEP-03	80	P
3566	TERMINAL SACRIFICE	1-SEP-03	76	P
3567	TERMINAL SACRIFICE	28-AUG-03	72	P
3568	TERMINAL SACRIFICE	29-AUG-03	73	P
3569	TERMINAL SACRIFICE	30-AUG-03	74	P
3570	TERMINAL SACRIFICE	31-AUG-03	75	P
3571	TERMINAL SACRIFICE	31-AUG-03	75	P
3572	TERMINAL SACRIFICE	29-AUG-03	73	P
3573	TERMINAL SACRIFICE	1-SEP-03	76	P
3574	TERMINAL SACRIFICE	28-AUG-03	72	P

NP-NOT PREGNANT, P-PREGNANT

5-FEB-2004 17:22

Huntingdon Life Sciences 03-4254

PAGE 124

APPENDIX B - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL ANIMAL TERMINATION HISTORY

FEMALES GROUP 4 400 MG/KG/DAY

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY	PREGNANCY STATUS
4563	TERMINAL SACRIFICE	29-AUG-03	73	P
4564	TERMINAL SACRIFICE	31-AUG-03	75	P
4565	TERMINAL SACRIFICE	30-AUG-03	74	P
4566	TERMINAL SACRIFICE	31-AUG-03	75	P
4567	TERMINAL SACRIFICE	31-AUG-03	75	P
4568	TERMINAL SACRIFICE	1-SEP-03	76	P
4569	TERMINAL SACRIFICE	29-AUG-03	73	P
4570	TERMINAL SACRIFICE	31-AUG-03	75	P
4571	TERMINAL SACRIFICE	31-AUG-03	75	P
4572	TERMINAL SACRIFICE	31-AUG-03	75	P
4573	TERMINAL SACRIFICE	30-AUG-03	74	P
4574	TERMINAL SACRIFICE	31-AUG-03	75	P

NP-NOT PREGNANT, P-PREGNANT

5-FEB-2004 17:22

Huntingdon Life Sciences 03-4254

PAGE 125

APPENDIX B - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL ANIMAL TERMINATION HISTORY

FEMALES GROUP 5 1000 MG/KG/DAY

ANIMAL#		TYPE OF DEATH	DATE OF DEATH	STUDY DAY	PREGNANCY STATUS
5563		TERMINAL SACRIFICE	31-AUG-03	75	P
5564		TERMINAL SACRIFICE	29-AUG-03	73	P
5565		TERMINAL SACRIFICE	1-SEP-03	76	P
5566		TERMINAL SACRIFICE	2-SEP-03	77	P
5567		TERMINAL SACRIFICE	31-AUG-03	75	P
5568		TERMINAL SACRIFICE	30-AUG-03	74	P
5569		TERMINAL SACRIFICE	31-AUG-03	75	P
5570		TERMINAL SACRIFICE	28-AUG-03	72	P
5571	TLL	TERMINAL SACRIFICE	19-AUG-03	63	P
5572		TERMINAL SACRIFICE	14-AUG-03	58	NP
5573		TERMINAL SACRIFICE	31-AUG-03	75	P
5574		TERMINAL SACRIFICE	29-AUG-03	73	P

NP-NOT PREGNANT, P-PREGNANT

TLL=TOTAL LITTER LOSS

5-FEB-2004 17:24

Huntingdon Life Sciences 03-4254

PAGE 126

APPENDIX C - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL WEEKLY CLINICAL OBSERVATIONS

MALES GROUP 1 0 MG/KG/DAY

ANIMAL#	OBSERVATIONS	DAY OF STUDY	-	1	2	2	3	4	4	5	6	6	
			5	6	3	0	7	4	1	8	5	2	4
1063	WITHIN NORMAL LIMITS		P	P									
	TERMINAL SACRIFICE											P	
	ALOPECIA - EXTREMITIES/SNOUT				3	3	3	3	3	2	2	2	
1064	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	
	TERMINAL SACRIFICE												P
1065	WITHIN NORMAL LIMITS		P										
	TERMINAL SACRIFICE												P
	ULCERATION - CERVICAL			P	P	P	P	P	P	P	P	P	
	ALOPECIA - GENERAL				3	3	3	3	3	3	3	3	
	SCABS								P	P	P	P	
	CERVICAL												
1066	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	
	TERMINAL SACRIFICE												P
1067	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	
	TERMINAL SACRIFICE												P
1068	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	
	TERMINAL SACRIFICE												P
1069	WITHIN NORMAL LIMITS		P	P			P	P	P	P	P	P	
	TERMINAL SACRIFICE												P
	RED EXUDATE (GENERAL)				P								
	FROM PENIS												
1070	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	
	TERMINAL SACRIFICE												P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

5-FEB-2004 17:24

Huntingdon Life Sciences 03-4254

PAGE 127

APPENDIX C - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL WEEKLY CLINICAL OBSERVATIONS

MALES GROUP 1 0 MG/KG/DAY

ANIMAL#	OBSERVATIONS	DAY OF STUDY	-	1	2	2	3	4	4	5	6	6	
			5	6	3	0	7	4	1	8	5	2	4
1071	WITHIN NORMAL LIMITS		P	P	P	P	P		P	P	P	P	
	TERMINAL SACRIFICE												P
	INCISORS BROKEN/MISSING							P					
1072	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	
	TERMINAL SACRIFICE												P
1073	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	
	TERMINAL SACRIFICE												P
1074	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	
	TERMINAL SACRIFICE												P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX C - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL WEEKLY CLINICAL OBSERVATIONS

MALES GROUP 2 64 MG/KG/DAY

ANIMAL#	OBSERVATIONS	DAY OF STUDY	-	1	2	2	3	4	4	5	6	6	
			5	6	3	0	7	4	1	8	5	2	4
2063	WITHIN NORMAL LIMITS		P										
	TERMINAL SACRIFICE												P
	ALOPECIA - EXTREMITIES/SNOUT			3	3	3	3	3	3	2	2	2	
2064	WITHIN NORMAL LIMITS		P	P	P	P	P		P	P	P	P	
	TERMINAL SACRIFICE												P
	CHROMODACRYORRHEA - BILATERAL								P				
	INCISORS BROKEN/MISSING								P				
2065	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P			
	TERMINAL SACRIFICE												P
	ALOPECIA - EXTREMITIES/SNOUT										3	3	
2066	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	
	TERMINAL SACRIFICE												P
2067	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	
	TERMINAL SACRIFICE												P
2068	WITHIN NORMAL LIMITS		P	P									
	TERMINAL SACRIFICE												P
	ALOPECIA - EXTREMITIES/SNOUT				3	3	3	3	3	3	3	3	
2069	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	
	TERMINAL SACRIFICE												P
2070	WITHIN NORMAL LIMITS		P										
	TERMINAL SACRIFICE												P
	ALOPECIA - EXTREMITIES/SNOUT					3	3	3	3	3	3	3	
	ULCERATION			P									
	RIGHT UPPER LAT												
	ULCERATION - CERVICAL			P									
	ALOPECIA - GENERAL				3								
	SCABS				P								
	CERVICAL												

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

5-FEB-2004 17:24

Huntingdon Life Sciences 03-4254

PAGE 129

APPENDIX C - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL WEEKLY CLINICAL OBSERVATIONS

MALES GROUP 2 64 MG/KG/DAY

ANIMAL#	OBSERVATIONS	DAY OF	-	1	2	2	3	4	4	5	6	6
		STUDY	5	6	3	0	7	4	1	8	5	2
2071	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	
	TERMINAL SACRIFICE											P
2072	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	
	TERMINAL SACRIFICE											P
2073	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	
	TERMINAL SACRIFICE											P
2074	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	
	TERMINAL SACRIFICE											P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX C - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL WEEKLY CLINICAL OBSERVATIONS

MALES GROUP 3 160 MG/KG/DAY

ANIMAL#	OBSERVATIONS	DAY OF STUDY	-	1	2	2	3	4	4	5	6	6
			5	6	3	0	7	4	1	8	5	2
3063	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P	P	P	P	P	P	P	P	P	P
3064	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P	P	P	P	P	P	P	P	P	P
3065	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P	P	P	P	P	P	P	P	P	P
3066	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P	P	P	P	P	P	P	P	P	P
3067	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P	P	P	P	P	P	P	P	P	P
3068	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P	P	P	P	P	P	P	P	P	P
3069	WITHIN NORMAL LIMITS TERMINAL SACRIFICE ALOPECIA - EXTREMITIES/SNOUT		P	P	P	P	P	P	P			
3070	WITHIN NORMAL LIMITS TERMINAL SACRIFICE CHROMODACRYORRHEA - UNILATERAL LACRIMATION - UNILATERAL INCISORS MALOCCLUDED INCISORS BROKEN/MISSING		P	P	P							
3071	WITHIN NORMAL LIMITS TERMINAL SACRIFICE ALOPECIA - EXTREMITIES/SNOUT INCISORS MALOCCLUDED INCISORS BROKEN/MISSING		P	P	P							

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

5-FEB-2004 17:24

Huntingdon Life Sciences 03-4254

PAGE 131

APPENDIX C - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL WEEKLY CLINICAL OBSERVATIONS

MALES GROUP 3 160 MG/KG/DAY

ANIMAL#	OBSERVATIONS	DAY OF	-	1	2	2	3	4	4	5	6	6
		STUDY	5	6	3	0	7	4	1	8	5	2
3072	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	
	TERMINAL SACRIFICE											P
3073	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	
	TERMINAL SACRIFICE											P
3074	WITHIN NORMAL LIMITS		P			P	P	P	P	P	P	
	TERMINAL SACRIFICE											P
	RAPID BREATHING			P	P							

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX C - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL WEEKLY CLINICAL OBSERVATIONS

MALES GROUP 4 400 MG/KG/DAY

ANIMAL#	OBSERVATIONS	DAY OF	-	1	2	2	3	4	4	5	6	6
		STUDY	5	6	3	0	7	4	1	8	5	2
4063	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	
	TERMINAL SACRIFICE											P
4064	WITHIN NORMAL LIMITS		P	P								
	TERMINAL SACRIFICE											P
	ALOPECIA - EXTREMITIES/SNOUT				3	3	3	3	2	2	2	2
4065	WITHIN NORMAL LIMITS		P	P	P	P						
	TERMINAL SACRIFICE											P
	ALOPECIA - EXTREMITIES/SNOUT						3	3	3	3	3	3
4066	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	
	TERMINAL SACRIFICE											P
4067	WITHIN NORMAL LIMITS		P	P	P							
	TERMINAL SACRIFICE											P
	ALOPECIA - EXTREMITIES/SNOUT					3	3	3	3	3	3	3
4068	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	
	TERMINAL SACRIFICE											P
4069	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	
	TERMINAL SACRIFICE											P
4070	WITHIN NORMAL LIMITS		P	P								
	TERMINAL SACRIFICE											P
	ALOPECIA - EXTREMITIES/SNOUT				3	3	3	3	3	3	3	3
4071	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	
	TERMINAL SACRIFICE											P
	ALOPECIA - EXTREMITIES/SNOUT											2
CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT												

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

5-FEB-2004 17:24

Huntingdon Life Sciences 03-4254

PAGE 133

APPENDIX C - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL WEEKLY CLINICAL OBSERVATIONS

MALES GROUP 4 400 MG/KG/DAY

ANIMAL#	OBSERVATIONS	DAY OF STUDY	-	1	2	2	3	4	4	5	6	6
4072	WITHIN NORMAL LIMITS		P	P	P							
	TERMINAL SACRIFICE											P
	ALOPECIA - EXTREMITIES/SNOUT				2	3	3	3	3	3	2	
4073	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P
	TERMINAL SACRIFICE											P
4074	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P
	TERMINAL SACRIFICE											P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

5-FEB-2004 17:24

Huntingdon Life Sciences 03-4254

PAGE 134

APPENDIX C - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL WEEKLY CLINICAL OBSERVATIONS

MALES GROUP 5 1000 MG/KG/DAY

ANIMAL#	OBSERVATIONS	DAY OF STUDY	-	1	2	2	3	4	4	5	6	6	
			5	6	3	0	7	4	1	8	5	2	4
5063	WITHIN NORMAL LIMITS		P	P									
	TERMINAL SACRIFICE										P		
	SWOLLEN PAW(S)						P	P	P	P	P		
	RIGHT FOREPAW												
	ALOPECIA - EXTREMITIES/SNOUT				3	3	3	3	3	3	3	3	
5064	WITHIN NORMAL LIMITS		P										
	TERMINAL SACRIFICE										P		
	ALOPECIA - EXTREMITIES/SNOUT				3	3	3	3	2	3	3	3	
	RAPID BREATHING		P	P									
5065	WITHIN NORMAL LIMITS		P										
	TERMINAL SACRIFICE										P		
	SWOLLEN DIGIT										P		
	R FOREPAW												
	ALOPECIA - EXTREMITIES/SNOUT				2	3	3	3	3	3	3	3	
	INCREASED VOCALIZATION		P	P	P	P	P	P	P	P	P	P	
5066	WITHIN NORMAL LIMITS		P					P	P	P	P	P	
	TERMINAL SACRIFICE											P	
	RAPID BREATHING		P	P	P	P							
5067	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	
	TERMINAL SACRIFICE											P	
5068	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P		P	P	
	TERMINAL SACRIFICE											P	
	CHROMODACRYORRHEA - UNILATERAL									P			
	LACRIMATION - UNILATERAL									2			
CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT													

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

5-FEB-2004 17:24

Huntingdon Life Sciences 03-4254

PAGE 135

APPENDIX C - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL WEEKLY CLINICAL OBSERVATIONS.

MALES GROUP 5 1000 MG/KG/DAY

ANIMAL#	OBSERVATIONS	DAY OF STUDY	-	1	2	2	3	4	4	5	6	6	
			5	6	3	0	7	4	1	8	5	2	4
5069	WITHIN NORMAL LIMITS		P	P									
	TERMINAL SACRIFICE											P	
	INCREASED VOCALIZATION				P	P	P	P	P	P	P	P	
	RAPID BREATHING				P	P	P						
	RALES - MOIST						P	P					
5070	WITHIN NORMAL LIMITS		P	P	P				P	P	P	P	
	TERMINAL SACRIFICE												P
	INCREASED VOCALIZATION						P	P	P				
5071	WITHIN NORMAL LIMITS		P					P	P				
	TERMINAL SACRIFICE												P
	ALOPECIA - EXTREMITIES/SNOUT											3	
	INCREASED VOCALIZATION				P	P	P		P	P	P		
	RAPID BREATHING				P	P	P	P					
5072	WITHIN NORMAL LIMITS		P	P			P	P	P	P	P	P	
	TERMINAL SACRIFICE												P
	RAPID BREATHING						P						
5073	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	
	TERMINAL SACRIFICE												P
5074	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P		
	TERMINAL SACRIFICE												P
	INCREASED VOCALIZATION											P	

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

5-FEB-2004 17:43

Huntingdon Life Sciences 03-4254

PAGE 136

APPENDIX C - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL WEEKLY CLINICAL OBSERVATIONS

FEMALES GROUP 1 0 MG/KG/DAY

ANIMAL#	OBSERVATIONS	DAY OF STUDY	-	1	2	2	3	4	4	
			5	6	3	0	7	4	1	8
1563	WITHIN NORMAL LIMITS		P	P	P	P	P			
1564	WITHIN NORMAL LIMITS		P	P	P	P	P	P		
1565	WITHIN NORMAL LIMITS		P	P	P	P	P			
1566	WITHIN NORMAL LIMITS		P	P	P	P	P			
1567	WITHIN NORMAL LIMITS ALOPECIA - EXTREMITIES/SNOUT		P	P						
					2	2	2			
1568	WITHIN NORMAL LIMITS		P	P	P	P	P			
1569	WITHIN NORMAL LIMITS		P	P	P	P	P			
1570	WITHIN NORMAL LIMITS		P	P	P	P	P			
1571	WITHIN NORMAL LIMITS		P	P	P	P	P			
1572	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P
1573	WITHIN NORMAL LIMITS		P	P	P	P	P			
1574	WITHIN NORMAL LIMITS		P	P	P	P	P			

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

5-FEB-2004 17:43

Huntingdon Life Sciences 03-4254

PAGE 137

APPENDIX C - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL WEEKLY CLINICAL OBSERVATIONS

FEMALES GROUP 2 64 MG/KG/DAY

ANIMAL#	OBSERVATIONS	DAY OF STUDY	-	1	2	2	3	4	4			
			5	6	3	0	7	4	1	8		
2563	WITHIN NORMAL LIMITS ULCERATION - CERVICAL TREMORS		P		P	P			P			
2564	WITHIN NORMAL LIMITS		P	P	P	P	P	P				
2565	WITHIN NORMAL LIMITS		P	P	P	P	P	P				
2566	WITHIN NORMAL LIMITS		P	P	P	P	P	P				
2567	WITHIN NORMAL LIMITS		P	P	P	P	P	P				
2568	WITHIN NORMAL LIMITS		P	P	P	P	P	P				
2569	WITHIN NORMAL LIMITS ALOPECIA - EXTREMITIES/SNOUT		P	P			3	3	3	3	2	2
2570	WITHIN NORMAL LIMITS		P	P	P	P	P	P				
2571	WITHIN NORMAL LIMITS		P	P	P	P	P	P				
2572	WITHIN NORMAL LIMITS		P	P	P	P	P	P				
2573	WITHIN NORMAL LIMITS INCREASED ACTIVITY		P		P	P	P	P				
2574	WITHIN NORMAL LIMITS		P	P	P	P	P	P				

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

5-FEB-2004 17:43

Huntingdon Life Sciences 03-4254

PAGE 138

APPENDIX C - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL WEEKLY CLINICAL OBSERVATIONS

FEMALES GROUP 3 160 MG/KG/DAY

ANIMAL#	OBSERVATIONS	DAY OF STUDY	-	1	2	2	3	4	4
			5	6	3	0	7	4	1 8
3563	WITHIN NORMAL LIMITS RAPID BREATHING		P		P	P			
3564	WITHIN NORMAL LIMITS		P	P	P	P	P		
3565	WITHIN NORMAL LIMITS		P	P	P	P	P	P	
3566	WITHIN NORMAL LIMITS		P	P	P	P	P		
3567	WITHIN NORMAL LIMITS		P	P	P	P	P		
3568	WITHIN NORMAL LIMITS		P	P	P	P	P		
3569	WITHIN NORMAL LIMITS INCREASED ACTIVITY RAPID BREATHING		P		P	P			
3570	WITHIN NORMAL LIMITS		P	P	P	P	P		
3571	WITHIN NORMAL LIMITS INCREASED ACTIVITY		P		P	P	P		
3572	WITHIN NORMAL LIMITS		P	P	P	P	P		
3573	WITHIN NORMAL LIMITS		P	P	P	P	P		
3574	WITHIN NORMAL LIMITS INCREASED ACTIVITY RAPID BREATHING		P		P	P			

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX C - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL WEEKLY CLINICAL OBSERVATIONS

FEMALES GROUP 4 400 MG/KG/DAY

ANIMAL#	OBSERVATIONS	DAY OF STUDY	-	1	2	2	3	4	4
			5	6	3	0	7	4	1 8
4563	WITHIN NORMAL LIMITS		P	P	P	P	P		
4564	WITHIN NORMAL LIMITS		P	P	P	P	P		
4565	WITHIN NORMAL LIMITS		P			P	P		
	TREMORS			P					
	INCREASED ACTIVITY			P					
	RAPID BREATHING			P	P				
4566	WITHIN NORMAL LIMITS		P	P	P	P	P		
4567	WITHIN NORMAL LIMITS		P	P		P	P		
	RAPID BREATHING				P				
4568	WITHIN NORMAL LIMITS		P		P	P			
	ALOPECIA - EXTREMITIES/SNOUT							3	
	INCREASED ACTIVITY			P					
4569	WITHIN NORMAL LIMITS		P	P	P	P	P		
4570	WITHIN NORMAL LIMITS		P	P		P	P		
	RAPID BREATHING				P				
4571	WITHIN NORMAL LIMITS		P				P		
	INCREASED ACTIVITY			P					
	IRREGULAR GAIT			P					
	RAPID BREATHING			P	P	P			
4572	WITHIN NORMAL LIMITS		P	P					
	INCREASED VOCALIZATION				P				
	RAPID BREATHING				P	P	P		

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

5-FEB-2004 17:43

Huntingdon Life Sciences 03-4254

PAGE 140

APPENDIX C - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL WEEKLY CLINICAL OBSERVATIONS

FEMALES GROUP 4 400 MG/KG/DAY

ANIMAL#	OBSERVATIONS	DAY OF STUDY	-	1	2	2	3	4	4
4573	WITHIN NORMAL LIMITS		5	6	3	0	7	4	1
4574	WITHIN NORMAL LIMITS								
	RAPID BREATHING								

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

5-FEB-2004 17:43

Huntingdon Life Sciences 03-4254

PAGE 141

APPENDIX C - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL WEEKLY CLINICAL OBSERVATIONS

FEMALES GROUP 5 1000 MG/KG/DAY

ANIMAL#	OBSERVATIONS	DAY OF STUDY	-	1	2	2	3	4	4
			5	6	3	0	7	4	1
			8						
5563	WITHIN NORMAL LIMITS		P	P					
	INCREASED ACTIVITY			P					
	RAPID BREATHING			P	P	P			
5564	WITHIN NORMAL LIMITS		P	P	P	P	P		
5565	WITHIN NORMAL LIMITS		P	P	P	P	P		
5566	WITHIN NORMAL LIMITS		P	P	P	P	P		
5567	WITHIN NORMAL LIMITS		P	P	P	P	P		
5568	WITHIN NORMAL LIMITS		P	P	P	P	P		
5569	WITHIN NORMAL LIMITS		P						
	ALOPECIA - EXTREMITIES/SNOUT			3	3	3	3		
	INCREASED ACTIVITY			P					
	INCREASED VOCALIZATION				P	P	P		
	RAPID BREATHING			P					
5570	WITHIN NORMAL LIMITS		P	P	P	P	P		
5571	WITHIN NORMAL LIMITS		P	P	P	P	P		
5572	WITHIN NORMAL LIMITS		P	P	P	P	P		
5573	WITHIN NORMAL LIMITS		P			P	P		
	RAPID BREATHING			P	P				
5574	WITHIN NORMAL LIMITS		P	P					
	ALOPECIA - EXTREMITIES/SNOUT			2	2	2			

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

	Individual Daily and Post-Dose Observations F ₀ Generation Preface	Appendix D
--	---	------------

Viability Observations and/or Clinical Signs (Cage-Side) - Animals were observed for mortality, morbidity, and signs of severe toxicity twice daily. Only animals with abnormal observations are listed in this appendix. Animals which were within normal limits are not included in this appendix. The last days of observations for F₀ males and females (prior to necropsy) were Day 63 and 79, respectively.

Post-Dose Observations - Each animal was checked for overt signs of toxicity prior to dosing and any changes from the preceding observation were recorded. Each dosed animal was then observed approximately one to two hours after dosing. Additional observations were made as appropriate (at 4 hours after dosing during the first 4 days of dosing).

Note:

All of the above observations were combined into the following appendix.

Males	Individual Daily and Post-Dose Observations F ₀ Generation	Appendix D
-------	--	------------

Animal		STUDY DAY																							
Number	Observations	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
Group 4 - 400 mg/kg/day																									
4070	Low Arousal	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	P	-	-	-	-	-	-
Group 5 - 1000 mg/kg/day																									
All	Ataxia	P	P	P	P	P	P	P	P	P	P	-	-	-	-	-	-	P	P	-	-	-	-	P	P
	Decreased Activity	P	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	Decreased Responsiveness	P	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	Lethargic	P	P	P	P	P	P	P	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	Irregular Gait	P	P	P	P	P	P	P	P	P	P	P	-	-	-	-	-	-	P	P	P	P	P	P	P
	Low Arousal	-	P	P	P	P	P	P	-	-	P	-	-	-	P	P	P	P	P	P	P	P	P	P	P
5064	Ataxia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	P	P	P	-	-	-
	Low Arousal	-	-	-	-	-	-	-	-	-	-	-	-	P	-	-	-	-	-	-	-	-	-	-	-
5065	Irregular Gait	-	-	-	-	-	-	-	-	-	-	-	P	-	-	-	-	-	-	-	-	-	-	-	-
	Ataxia	-	-	-	-	-	-	-	-	-	-	-	P	-	P	P	P	-	-	P	P	P	P	-	-
	Low Arousal	-	-	-	-	-	-	-	-	-	-	-	-	P	-	-	-	-	-	-	-	-	-	-	-
5066	Ataxia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	P	P	-	-	P	-	P	-	-	-
5067	Irregular Gait	-	-	-	-	-	-	-	-	-	-	-	P	-	-	-	-	-	-	-	-	-	-	-	-
	Ataxia	-	-	-	-	-	-	-	-	-	-	-	P	-	-	P	P	-	P	P	P	P	P	-	-
	Low Arousal	-	-	-	-	-	-	-	-	-	-	-	-	P	-	-	-	-	-	-	-	-	-	-	-
5068	Ataxia	-	-	-	-	-	-	-	-	-	-	-	-	-	P	P	P	-	P	P	P	P	P	-	-
5069	Ataxia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	P	-	-	-	-	-	P	P	-	-
5070	Ataxia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	P	P	-	-	-	-	P	-	-	-

KEY: P=Present at PM observation. ✓ = Present at both AM and PM observation.

Males	Individual Daily and Post-Dose Observations F ₀ Generation	Appendix D
-------	--	------------

Animal		STUDY DAY																							
Number Observations		0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
Group 5 - 1000 mg/kg/day																									
5071	Ataxia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	P	-	-	P	P	P	-	-	-
5072	Ataxia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	P	-	-	P	P	P	-	-	-
	Low Arousal	-	-	-	-	-	-	-	-	-	-	-	-	P	-	-	-	-	-	-	-	-	-	-	-
5073	Ataxia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	P	P	-	-	-
5074	Ataxia	-	-	-	-	-	-	-	-	-	-	-	-	-	P	P	P	-	-	P	P	P	-	-	-
	Low Arousal	-	-	-	-	-	-	-	-	-	-	-	-	P	-	-	-	-	-	-	-	-	-	-	-

KEY: P=Present at PM observation. ✓ = Present at both AM and PM observation.

Males	Individual Daily and Post-Dose Observations F ₀ Generation	Appendix D
-------	--	------------

Animal		STUDY DAY																							
Number	Observations	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47
Group 5 - 1000 mg/kg/day																									
All	Ataxia	-	-	-	-	-	-	-	P	-	-	-	P	P	P	P	P	P	P	P	P	P	P	P	-
	Lethargic	-	-	-	-	-	-	-	-	-	-	-	P	-	-	-	-	-	-	-	-	-	-	-	-
	Irregular Gait	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	Low Arousal	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	-
5063	Ataxia	-	P	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5064	Ataxia	-	-	-	P	-	P	P	-	-	-	P	-	-	-	-	-	-	-	-	-	-	-	-	P
5065	Ataxia	P	P	P	P	P	P	P	-	-	P	P	-	-	-	-	-	-	-	-	-	-	-	-	P
5066	Ataxia	-	-	P	P	-	P	P	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	P
5067	Ataxia	P	P	P	P	P	P	P	-	-	P	P	-	-	-	-	-	-	-	-	-	-	-	-	P
5068	Ataxia	P	-	P	P	P	P	P	-	-	P	P	-	-	-	-	-	-	-	-	-	-	-	-	P
5069	Ataxia	-	-	P	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5070	Ataxia	-	-	-	P	P	P	P	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5071	Ataxia	-	-	-	-	P	-	P	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	P

KEY: P=Present at PM observation. ✓ = Present at both AM and PM observation.

Males	Individual Daily and Post-Dose Observations F ₀ Generation	Appendix D
-------	--	------------

Animal		STUDY DAY																							
Number	Observations	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47
Group 5 - 1000 mg/kg/day																									
5072	Ataxia	P	P	P	P	P	P	P	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5073	Ataxia	P	P	P	-	P	P	P	-	P	P	-	-	-	-	-	-	-	-	-	-	-	-	-	P
5074	Ataxia	P	P	P	P	P	P	P	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

KEY: P=Present at PM observation. ✓ = Present at both AM and PM observation.

Males	Individual Daily and Post-Dose Observations F ₀ Generation	Appendix D
-------	--	------------

Animal		STUDY DAY															
Number Observations		48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63
Group 5 - 1000 mg/kg/day																	
All	Ataxia	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	Irregular Gait	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	Low Arousal	P	P	P	P	P	P	P	P	P	P	P	P	P	-	-	P
5067	Low Arousal	-	-	-	-	-	-	-	-	-	-	-	-	-	P	P	-
	Lethargic	-	P	P	P	-	P	-	-	-	-	-	-	-	-	-	P
5068	Lethargic	-	P	P	P	-	P	-	-	-	-	-	-	-	-	-	P
	Low Arousal	-	-	-	-	-	-	-	-	-	-	-	-	-	P	P	P
5071	Low Arousal	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5072	Ataxia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5073	Ataxia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5074	Ataxia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

KEY: P=Present at PM observation. ✓ = Present at both AM and PM observation.

Females	Individual Daily and Post-Dose Observations F ₀ Generation	Appendix D
---------	--	------------

Animal		STUDY DAY																							
Number	Observations	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
Group 4 - 400 mg/kg/day																									
4569	Irregular Gait	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	P	-	-	-	P	P	-
4574	Ataxia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	P	-	P	-	-	-	-	-
	Irregular Gait	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	P	P	-
Group 5 - 1000 mg/kg/day																									
All	Ataxia	P	P	P	P	P	P	P	-	-	-	-	-	-	-	-	-	P	-	-	-	-	-	-	-
	Decreased Activity	P	P	-	-	-	-	P	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	Decreased Responsiveness	P	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	Low Arousal	-	P	P	P	P	P	P	P	P	-	-	-	-	P	P	P	-	P	P	P	P	P	P	P
	Irregular Gait	-	-	P	P	P	P	P	P	P	P	P	-	-	-	-	-	-	P	-	-	P	P	P	P
5563	Irregular Gait	P	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	Ataxia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	P	-	-	-	-	-	-
5564	Irregular Gait	P	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	Ataxia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	P	-	P	-	-	-	-	-	-
5565	Ataxia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	P	-	-	-	-	P	P
	"Hopped" with back legs	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	P	-	-	-	-	-	-	-
5566	Lethargic	P	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	Ataxia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	P	-	-	-	-	-	-	-	-	-
	Swollen eyelids	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	P	-	-	-	-	-	-	-
5570	Ataxia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	P	-	-	-	-	-	P	P	P	-

KEY: P=Present at PM observation. ✓ = Present at both AM and PM observation.

Females	Individual Daily and Post-Dose Observations F ₀ Generation	Appendix D
---------	--	------------

Animal	STUDY DAY																							
Number Observations	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
Group 5 - 1000 mg/kg/day																								
5571 Ataxia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	P	-	-	-	-	-	-
5572 Ataxia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	P	P	-	P	-	-	-	-	-	-
5574 Ataxia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	P	P	-	P	P	P	-	-	P	P
Swollen eyelids	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	P	-	-	-	-	-	-	-
Lacrimation - Bilateral	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	P	-	-	-	-	-	-	-

KEY: P=Present at PM observation. ✓ = Present at both AM and PM observation.

Females	Individual Daily and Post-Dose Observations F ₀ Generation	Appendix D
---------	--	------------

Animal		STUDY DAY																							
Number	Observations	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47
Group 4 - 400 mg/kg/day																									
4569	Irregular Gait	P	-	-	P	P	P	P	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Group 5 - 1000 mg/kg/day																									
All	Low Arousal	P	P	P	P	P	P	P	P	-	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	Irregular Gait	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
5563	Ataxia	-	-	-	-	-	-	-	P	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	P
5565	Ataxia	P	-	-	-	-	P	-	-	-	-	P	-	-	P	-	-	-	-	-	-	-	-	-	P
5566	Ataxia	-	-	-	-	-	P	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5567	Ataxia	P	-	-	-	-	-	-	-	-	-	-	-	-	P	P	-	P	-	-	P	P	P	-	-
5568	Ataxia	-	-	P	-	-	-	P	P	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5570	Ataxia	-	-	-	-	P	P	P	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5571	Ataxia	-	-	-	-	P	P	-	P	P	-	-	-	-	-	-	-	-	P	-	-	-	-	-	-
5572	Ataxia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5573	Ataxia	-	-	-	-	-	-	-	-	P	-	-	P	P	-	-	P	-	P	-	P	-	-	-	-
5574	Ataxia	-	P	P	P	P	P	-	-	-	-	-	-	P	P	P	P	P	P	P	P	P	P	P	P

KEY: P=Present at PM observation. ✓ = Present at both AM and PM observation.

Females	Individual Daily and Post-Dose Observations F ₀ Generation	Appendix D
---------	--	------------

Animal		STUDY DAY																							
Number	Observations	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	
Group 5	- 1000 mg/kg/day																								
All	Low Arousal	P	P	P	P	P	P	P	P	P	-	P	P	-	-	-	-	-	-	P	P	-	P	-	
	Irregular Gait	P	P	P	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
5563	Ataxia	P	-	-	-	-	-	-	-	P	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	Decreased Fecal Volume	-	-	-	-	-	-	-	-	P	P	-	-	-	-	-	-	-	-	-	-	-	-	-	
	Hypothermia	-	-	-	-	-	-	-	-	P	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	Pale	-	-	-	-	-	-	-	-	P	✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	
	Red exudate ano-genital Area	-	-	-	-	-	-	-	-	P	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
5565	Ataxia	-	-	-	-	-	-	-	-	-	P	P	-	-	-	-	-	-	-	-	-	-	-	-	
5566	Ataxia	-	-	-	-	-	-	-	-	-	P	-	-	-	-	-	-	-	-	-	-	-	-	-	
5568	Ataxia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	Lacrimation - Bilateral	-	-	-	P	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
5574	Ataxia	P	P	-	P	P	-	-	-	P	-	-	-	-	-	-	-	-	-	-	-	-	-	-	

KEY: P=Present at PM observation. ✓ = Present at both AM and PM observation.

Females	Individual Daily and Post-Dose Observations F ₀ Generation	Appendix D
---------	--	------------

Animal		STUDY DAY									
Number	Observations	71	72	73	74	75	76	77	78	79	
Groups 1-5											
All	Within Normal Limits	P	P	P	P	P	P	P	P	P	
(Remaining)											

KEY: P=Present at PM observation. ✓ = Present at both AM and PM observation.

5-FEB-2004 18:00

Huntingdon Life Sciences 03-4254

PAGE 153

APPENDIX E - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL CLINICAL OBSERVATIONS DURING GESTATION

GROUP 1 0 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF GESTATION	1 1 1 1 1 1 1 1 1 1 2																				
			0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0
1563	WITHIN NORMAL LIMITS		P							P							P						P
1564	WITHIN NORMAL LIMITS		P							P							P						P
1565	WITHIN NORMAL LIMITS		P							P							P						P
1566	WITHIN NORMAL LIMITS		P							P							P						P
1567	ALOPECIA - EXTREMITIES/SNOUT		2							2							2						3
1568	ALOPECIA - EXTREMITIES/SNOUT WITHIN NORMAL LIMITS									2							2						2
1569	WITHIN NORMAL LIMITS		P							P							P						P
1570	ALOPECIA - EXTREMITIES/SNOUT WITHIN NORMAL LIMITS									2							2						2
1571	WITHIN NORMAL LIMITS		P							P							P						P
1573	ALOPECIA - EXTREMITIES/SNOUT WITHIN NORMAL LIMITS																2						2
1574	WITHIN NORMAL LIMITS		P							P							P						P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX E - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL CLINICAL OBSERVATIONS DURING GESTATION

GROUP 2 64 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF GESTATION	1 1 1 1 1 1 1 1 1 1 2																							
			0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0			
2563	ALOPECIA - GENERAL WITHIN NORMAL LIMITS	3								P							P						P			
2564	CHROMODACRYORRHEA - UNILATERAL LACRIMATION - UNILATERAL INCISORS MALOCCLUDED	P 2 P								P							P						P			
2565	WITHIN NORMAL LIMITS	P								P							P						P			
2566	WITHIN NORMAL LIMITS	P								P							P						P			
2567	WITHIN NORMAL LIMITS	P								P							P						P			
2568	WITHIN NORMAL LIMITS	P								P							P						P			
2570	ALOPECIA - EXTREMITIES/SNOUT WITHIN NORMAL LIMITS	P								P							2						P			
2571	WITHIN NORMAL LIMITS	P								P							P						P			
2572	ALOPECIA - EXTREMITIES/SNOUT WITHIN NORMAL LIMITS	P								2							2						P			
2573	WITHIN NORMAL LIMITS	P								P							P						P			
2574	WITHIN NORMAL LIMITS	P								P							P						P			

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

5-FEB-2004 18:00

Huntingdon Life Sciences 03-4254

PAGE 155

APPENDIX E - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL CLINICAL OBSERVATIONS DURING GESTATION

GROUP 3 160 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF GESTATION	1 1 1 1 1 1 1 1 1 1 2																							
			0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0			
3563	WITHIN NORMAL LIMITS		P							P							P						P			
3564	WITHIN NORMAL LIMITS		P							P							P						P			
3565	WITHIN NORMAL LIMITS		P							P							P						P			
3566	WITHIN NORMAL LIMITS		P							P							P						P			
3567	WITHIN NORMAL LIMITS		P							P							P						P			
3568	WITHIN NORMAL LIMITS		P							P							P						P			
3569	WITHIN NORMAL LIMITS		P							P							P						P			
3570	WITHIN NORMAL LIMITS		P							P							P						P			
3571	WITHIN NORMAL LIMITS		P							P							P						P			
3572	WITHIN NORMAL LIMITS		P							P							P						P			
3573	WITHIN NORMAL LIMITS		P							P							P						P			
3574	WITHIN NORMAL LIMITS		P							P							P						P			
CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT																										

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

5-FEB-2004 18:00

Huntingdon Life Sciences 03-4254

PAGE 156

APPENDIX E - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL CLINICAL OBSERVATIONS DURING GESTATION

GROUP 4 400 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF GESTATION	1 1 1 1 1 1 1 1 1 2																							
			0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0			
4563	WITHIN NORMAL LIMITS		P							P							P						P			
4564	WITHIN NORMAL LIMITS		P							P							P						P			
4565	INCISORS BROKEN/MISSING WITHIN NORMAL LIMITS		P							P							P						P			
4566	WITHIN NORMAL LIMITS		P							P							P						P			
4567	WITHIN NORMAL LIMITS		P							P							P						P			
4568	ALOPECIA - EXTREMITIES/SNOUT		3							3							3						2			
4569	WITHIN NORMAL LIMITS		P							P							P						P			
4570	WITHIN NORMAL LIMITS		P							P							P						P			
4571	WITHIN NORMAL LIMITS		P							P							P						P			
4572	RAPID BREATHING WITHIN NORMAL LIMITS		P							P							P						P			
4573	WITHIN NORMAL LIMITS		P							P							P						P			
4574	ALOPECIA - EXTREMITIES/SNOUT		2							2							2						2			
CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT																										

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

5-FEB-2004 18:00

Huntingdon Life Sciences 03-4254

PAGE 157

APPENDIX E - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL CLINICAL OBSERVATIONS DURING GESTATION

GROUP 5 1000 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF GESTATION	1 1 1 1 1 1 1 1 1 1 2																							
			0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0			
5563	WITHIN NORMAL LIMITS		P							P							P						P			
5564	WITHIN NORMAL LIMITS		P							P							P						P			
5565	WITHIN NORMAL LIMITS		P							P							P						P			
5566	ALOPECIA - EXTREMITIES/SNOUT WITHIN NORMAL LIMITS		P							P							3						3			
5567	WITHIN NORMAL LIMITS		P							P							P						P			
5568	WITHIN NORMAL LIMITS		P							P							P						P			
5569	ALOPECIA - EXTREMITIES/SNOUT		3							2							3						3			
5570	WITHIN NORMAL LIMITS		P							P							P						P			
5571	WITHIN NORMAL LIMITS		P							P							P						P			
5572	WITHIN NORMAL LIMITS		P							P							P						P			
5573	WITHIN NORMAL LIMITS		P							P							P						P			
5574	ALOPECIA - EXTREMITIES/SNOUT		2							2							2						2			

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX F - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL MATERNAL CLINICAL OBSERVATIONS DURING LACTATION

GROUP 1 0 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF LACTATION	1 1 1 1 1 1 1 1 1 1 2 2																							
			0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0	1		
1563	WITHIN NORMAL LIMITS TERMINAL SACRIFICE			P						P						P								P		
																								P		
1564	WITHIN NORMAL LIMITS TERMINAL SACRIFICE			P						P						P								P		
																								P		
1565	WITHIN NORMAL LIMITS TERMINAL SACRIFICE			P						P						P								P		
																								P		
1566	WITHIN NORMAL LIMITS TERMINAL SACRIFICE			P						P						P								P		
																								P		
1568	TERMINAL SACRIFICE ALOPECIA - EXTREMITIES/SNOUT			2						2						2								P		
																								2		
1569	WITHIN NORMAL LIMITS TERMINAL SACRIFICE			P						P						P								P		
																								P		
1570	TERMINAL SACRIFICE ALOPECIA - EXTREMITIES/SNOUT			2						3						3								P		
																								2		
1571	WITHIN NORMAL LIMITS TERMINAL SACRIFICE			P						P						P								P		
																								P		
1572	WITHIN NORMAL LIMITS TERMINAL SACRIFICE			P						P						P								P		
																								P		
1573	WITHIN NORMAL LIMITS TERMINAL SACRIFICE ALOPECIA - EXTREMITIES/SNOUT			2						3						3								P		
																								P		

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

5-FEB-2004 18:43

Huntingdon Life Sciences 03-4254

PAGE 159

APPENDIX F - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL MATERNAL CLINICAL OBSERVATIONS DURING LACTATION

GROUP 1 0 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF LACTATION																		
			0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7
1574	WITHIN NORMAL LIMITS																			
	TERMINAL SACRIFICE																			

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX F - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL MATERNAL CLINICAL OBSERVATIONS DURING LACTATION

GROUP 2 64 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF LACTATION	1 1 1 1 1 1 1 1 1 1 2 2																							
			0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0	1		
2563	WITHIN NORMAL LIMITS																									
	TERMINAL SACRIFICE																									
2564	TERMINAL SACRIFICE																									
	CHROMODACRYORRHEA - UNILATERAL																									
	INCISORS MALOCCLUDED																									
	INCISORS BROKEN/MISSING																									
2565	WITHIN NORMAL LIMITS																									
	TERMINAL SACRIFICE																									
2566	WITHIN NORMAL LIMITS																									
	TERMINAL SACRIFICE																									
2567	WITHIN NORMAL LIMITS																									
	TERMINAL SACRIFICE																									
2568	WITHIN NORMAL LIMITS																									
	TERMINAL SACRIFICE																									
2569	TERMINAL SACRIFICE																									
	ALOPECIA - EXTREMITIES/SNOUT																									
2570	WITHIN NORMAL LIMITS																									
	TERMINAL SACRIFICE																									
	ALOPECIA - EXTREMITIES/SNOUT																									
2571	WITHIN NORMAL LIMITS																									
	TERMINAL SACRIFICE																									
2573	WITHIN NORMAL LIMITS																									
	TERMINAL SACRIFICE																									

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

5-FEB-2004 18:43

Huntingdon Life Sciences 03-4254

PAGE 161

APPENDIX F - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL MATERNAL CLINICAL OBSERVATIONS DURING LACTATION

GROUP 2 64 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF LACTATION																	
			0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6
2574	WITHIN NORMAL LIMITS																		
	TERMINAL SACRIFICE																		
	ALOPECIA - EXTREMITIES/SNOUT																		

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX F - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL MATERNAL CLINICAL OBSERVATIONS DURING LACTATION

GROUP 3 160 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF LACTATION	1 1 1 1 1 1 1 1 1 1 2 2																	
			0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7
3563	WITHIN NORMAL LIMITS TERMINAL SACRIFICE				P					P							P			P
3564	WITHIN NORMAL LIMITS TERMINAL SACRIFICE				P					P							P			P
3565	WITHIN NORMAL LIMITS TERMINAL SACRIFICE				P					P							P			P
3566	WITHIN NORMAL LIMITS TERMINAL SACRIFICE				P					P							P			P
3567	WITHIN NORMAL LIMITS TERMINAL SACRIFICE				P					P							P			P
3568	WITHIN NORMAL LIMITS TERMINAL SACRIFICE				P					P							P			P
3569	WITHIN NORMAL LIMITS TERMINAL SACRIFICE				P					P							P			P
3570	WITHIN NORMAL LIMITS TERMINAL SACRIFICE				P					P							P			P
3571	WITHIN NORMAL LIMITS TERMINAL SACRIFICE				P					P							P			P
3572	WITHIN NORMAL LIMITS TERMINAL SACRIFICE				P					P							P			P
3573	WITHIN NORMAL LIMITS TERMINAL SACRIFICE				P					P							P			P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

5-FEB-2004 18:43

Huntingdon Life Sciences 03-4254

PAGE 163

APPENDIX F - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL MATERNAL CLINICAL OBSERVATIONS DURING LACTATION

GROUP 3 160 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF LACTATION	0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0	1
3574	WITHIN NORMAL LIMITS																							
	TERMINAL SACRIFICE																							

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX F - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL MATERNAL CLINICAL OBSERVATIONS DURING LACTATION

GROUP 4 400 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF LACTATION	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1																	
			0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7
4563	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P							P							P			P
4564	WITHIN NORMAL LIMITS TERMINAL SACRIFICE ALOPECIA - EXTREMITIES/SNOUT MASS BOTTOM LIP		P								2					2				P
4565	WITHIN NORMAL LIMITS TERMINAL SACRIFICE ALOPECIA - EXTREMITIES/SNOUT		P								3					3				P
4566	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P							P						P				P
4567	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P							P						P				P
4568	TERMINAL SACRIFICE ALOPECIA - EXTREMITIES/SNOUT			2						3						3				P
4569	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P							P						P				P
4570	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P							P						P				P
4571	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P							P						P				P
4572	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P							P						P				P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

5-FEB-2004 18:43

Huntingdon Life Sciences 03-4254

PAGE 165

APPENDIX F - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL MATERNAL CLINICAL OBSERVATIONS DURING LACTATION

GROUP 4 400 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF LACTATION	1 1 1 1 1 1 1 1 1 1 1 2 2													
			0	1	2	3	4	5	6	7	8	9	0	1	2	3
4573	WITHIN NORMAL LIMITS TERMINAL SACRIFICE				P					P					P	P
4574	TERMINAL SACRIFICE ALOPECIA - EXTREMITIES/SNOUT				3					3					3	3

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX F - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL MATERNAL CLINICAL OBSERVATIONS DURING LACTATION

GROUP 5 1000 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF LACTATION	1 1 1 1 1 1 1 1 1 1 2 2																							
			0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0	1		
5563	WITHIN NORMAL LIMITS TERMINAL SACRIFICE			P						P							P							P		
																								P		
5564	WITHIN NORMAL LIMITS TERMINAL SACRIFICE			P						P							P							P		
																								P		
5565	TERMINAL SACRIFICE ALOPECIA - EXTREMITIES/SNOUT				2					3							3							P		
																								3		
5566	TERMINAL SACRIFICE ALOPECIA - EXTREMITIES/SNOUT				3					3							3							P		
																								3		
5567	WITHIN NORMAL LIMITS TERMINAL SACRIFICE			P						P							P							P		
																								P		
5568	WITHIN NORMAL LIMITS TERMINAL SACRIFICE			P						P							P							P		
																								P		
5569	TERMINAL SACRIFICE ALOPECIA - EXTREMITIES/SNOUT				3					3							3							P		
																								3		
5570	WITHIN NORMAL LIMITS TERMINAL SACRIFICE			P						P							P							P		
																								P		
5571	WITHIN NORMAL LIMITS TERMINAL SACRIFICE			P							P															
												P														
5573	WITHIN NORMAL LIMITS TERMINAL SACRIFICE ALOPECIA - EXTREMITIES/SNOUT			P						P							P							P		
																								3		

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

5-FEB-2004 18:43

Huntingdon Life Sciences 03-4254

PAGE 167

APPENDIX F - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL MATERNAL CLINICAL OBSERVATIONS DURING LACTATION

GROUP 5 1000 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF LACTATION	0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0	1	2	2
5574	TERMINAL SACRIFICE																									P
	ALOPECIA - EXTREMITIES/SNOUT				2					3							3									3

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

Huntingdon Life Sciences 03-4254

PAGE168

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

[illegible]

[illegible]

PAGE171

APPENDIX G - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL BODY WEIGHTS (GRAMS)

MALES GROUP 5 1000 MG/KG/DAY

[illegible]

5-FEB-2004 18:46

Huntingdon Life Sciences 03-4254

PAGE173

APPENDIX G - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

FEMALES GROUP 1		0 MG/KG/DAY									
		INDIVIDUAL BODY WEIGHTS (GRAMS)									

ANIMAL#	DAY OF STUDY										
	-5	0	6	13	20	27	34	41	48	55	62

1563	185	201	226	214	239	247					
1564	190	202	233	243	251	250	271				
1565	176	193	202	213	225	236					
1566	179	204	224	243	258	260					
1567	170	188	201	221	230	230				309	
1568	161	170	176	177	188	194					
1569	187	206	224	238	243	256					
1570	178	200	216	216	237	250					
1571	173	198	218	236	248	252					
1572	182	207	228	231	250	261	284	318	337		
1573	191	213	222	220	236	248					
1574	183	204	224	237	244	258					
MEAN	180	199	216	224	237	245	277	318	337	309	
S.D.	8.7	11.2	16.0	18.5	18.1	18.5	9.1	0.0	0.0	0.0	
N	12	12	12	12	12	12	2	1	1	1	

5-FEB-2004 18:46

Huntingdon Life Sciences 03-4254

PAGE174

APPENDIX G - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

		INDIVIDUAL BODY WEIGHTS (GRAMS)										
FEMALES	GROUP 2	64 MG/KG/DAY										

		DAY OF STUDY										
ANIMAL#		-5	0	6	13	20	27	34	41	48	55	62

2563		183	210	217	239	255	270					
2564		190	219	239	254	273	283					
2565		181	202	215	226	241	253					
2566		166	180	190	190	200	208					
2567		173	196	212	220	235	240					
2568		178	188	210	224	225	236					
2569		184	199	203	233	241	251	265	295	340		
2570		192	221	249	253	274	287					
2571		188	210	230	239	252	261					
2572		176	197	234	266	245	251					
2573		169	191	200	227	245	255					
2574		180	201	227	262	242	229					
MEAN		180	201	219	236	244	252	265	295	340		
S.D.		8.0	12.4	17.4	21.2	19.8	22.3	0.0	0.0	0.0		
N		12	12	12	12	12	12	1	1	1		

5-FEB-2004 18:46

Huntingdon Life Sciences 03-4254

PAGE175

APPENDIX G - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

		INDIVIDUAL BODY WEIGHTS (GRAMS)										
FEMALES	GROUP 3	160 MG/KG/DAY										
<hr/>												
		DAY	OF STUDY									
ANIMAL#		-5	0	6	13	20	27	34	41	48	55	62
<hr/>												
3563		184	206	207	232	237	249					
3564		185	209	213	237	234	253					
3565		181	193	209	219	225	228	256				
3566		179	206	227	241	248	256					
3567		174	189	196	201	216	222					
3568		179	193	193	205	221	224					
3569		172	198	203	220	226	243					
3570		159	165	179	190	188	199					
3571		190	206	229	233	257	266					
3572		169	186	199	214	228	238					
3573		182	203	228	254	253	264					
3574		201	218	239	248	273	286					
MEAN		180	198	210	224	234	244	256				
S.D.		10.6	13.9	17.6	19.8	22.2	23.7	0.0				
N		12	12	12	12	12	12	1				

5-FEB-2004 18:46

Huntingdon Life Sciences 03-4254

PAGE176

APPENDIX G - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

		INDIVIDUAL BODY WEIGHTS (GRAMS)										
FEMALES	GROUP 4	400 MG/KG/DAY										
		DAY OF STUDY										
ANIMAL#		-5	0	6	13	20	27	34	41	48	55	62
4563		179	201	210	227	237	236					
4564		176	183	199	215	212	224					
4565		190	211	209	233	248	248					
4566		169	185	188	201	212	223					
4567		171	189	205	206	229	228					
4568		182	205	220	245	259	276					
4569		184	212	224	237	255	266					
4570		178	204	225	226	248	245					
4571		162	183	179	194	198	204					
4572		186	205	204	234	240	259					
4573		181	200	218	220	248	257					
4574		194	209	229	245	244	261					
MEAN		179	199	209	223	236	244					
S.D.		9.0	11.0	15.2	16.7	19.2	21.3					
N		12	12	12	12	12	12					

5-FEB-2004 18:46

Huntingdon Life Sciences 03-4254

PAGE177

APPENDIX G - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

FEMALES GROUP 5		1000 MG/KG/DAY									
		INDIVIDUAL BODY WEIGHTS (GRAMS)									

ANIMAL#	DAY OF STUDY										
	-5	0	6	13	20	27	34	41	48	55	62

5563	166	191	204	206	232	231					
5564	174	202	200	227	242	246					
5565	177	202	213	232	255	264					
5566	189	218	223	232	248	262					
5567	168	189	197	219	236	237					
5568	195	235	239	253	274	290					
5569	180	197	197	210	204	220					
5570	185	211	224	235	256	271					
5571	182	194	200	213	223	236					264
5572	176	191	198	193	209	206					
5573	188	200	216	227	245	265					
5574	182	198	209	207	226	233					
MEAN	180	202	210	221	237	247					264
S.D.	8.6	13.5	13.5	16.2	20.2	23.9					0.0
N	12	12	12	12	12	12					1

5-FEB-2004 18:49

Huntingdon Life Sciences 03-4254

PAGE178

APPENDIX H - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL BODY WEIGHT GAIN (GRAMS)

MALES GROUP 1 0 MG/KG/DAY

[illegible]

[illegible]

5-FEB-2004 18:49

Huntingdon Life Sciences 03-4254

PAGE180

APPENDIX H - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL BODY WEIGHT GAIN (GRAMS)

MALES GROUP 3 160 MG/KG/DAY

[illegible]

5-FEB-2004 18:49

Huntingdon Life Sciences 03-4254

PAGE181

APPENDIX H - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL BODY WEIGHT GAIN (GRAMS)

MALES GROUP 4 400 MG/KG/DAY

[illegible]

5-FEB-2004 18:49

Huntingdon Life Sciences 03-4254

PAGE182

APPENDIX H - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL BODY WEIGHT GAIN (GRAMS)

MALES GROUP 5 1000 MG/KG/DAY

[illegible]

5-FEB-2004 18:55

Huntingdon Life Sciences 03-4254

PAGE183

APPENDIX H - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

FEMALES GROUP 1 0 MG/KG/DAY

INDIVIDUAL BODY WEIGHT GAIN (GRAMS)

ANIMAL#	DAY OF STUDY								
	-5-0	0-6	6-13	13-20	20-27	27-34	34-41	41-48	0-27
1563	16	25	-13	25	8				46
1564	12	31	10	8	-1	21			48
1565	17	9	11	12	12				43
1566	25	20	18	15	3				56
1567	18	13	21	8	0				42
1568	9	6	2	11	6				25
1569	19	18	14	5	12				50
1570	22	16	0	21	13				50
1571	26	20	18	12	4				54
1572	24	22	3	19	11	22	34	19	55
1573	22	9	-2	15	12				35
1574	21	20	13	7	13				53
MEAN	19	17	8	13	8	22	34	19	46
S.D.	5.3	7.3	9.9	6.1	5.4	0.8	0.0	0.0	9.2
N	12	12	12	12	12	2	1	1	12

5-FEB-2004 18:55

Huntingdon Life Sciences 03-4254

PAGE184

APPENDIX H - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

FEMALES GROUP 2 64 MG/KG/DAY

INDIVIDUAL BODY WEIGHT GAIN (GRAMS)

ANIMAL#	DAY OF STUDY								
	-5-0	0-6	6-13	13-20	20-27	27-34	34-41	41-48	0-27
2563	27	7	21	16	15				60
2564	30	20	15	18	10				63
2565	21	13	11	15	13				51
2566	13	10	0	10	8				28
2567	23	15	8	16	4				43
2568	9	23	14	1	11				48
2569	15	4	29	8	11	14	30	45	52
2570	29	28	4	20	13				67
2571	23	19	9	13	9				51
2572	21	38	32	-20	6				55
2573	22	9	26	19	10				63
2574	21	27	34	-20	-12				28
MEAN	21	18	17	8	8	14	30	45	51
S.D.	6.2	9.9	11.3	14.2	7.1	0.0	0.0	0.0	12.5
N	12	12	12	12	12	1	1	1	12

5-FEB-2004 18:55

Huntingdon Life Sciences 03-4254

PAGE185

APPENDIX H - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL BODY WEIGHT GAIN (GRAMS)									
FEMALES GROUP 3 160 MG/KG/DAY									
ANIMAL#	DAY OF STUDY								
	-5-0	0-6	6-13	13-20	20-27	27-34	34-41	41-48	0-27
3563	23	1	25	4	12				42
3564	23	5	24	-3	19				45
3565	12	17	9	6	3	28			35
3566	28	21	14	7	8				50
3567	15	8	5	15	5				33
3568	14	0	12	17	3				32
3569	27	5	17	7	17				45
3570	6	14	11	-2	11				34
3571	16	22	4	24	10				60
3572	17	13	15	14	10				52
3573	21	24	27	-1	11				60
3574	17	21	9	26	13				69
MEAN	18	13	14	9	10	28			46
S.D.	6.4	8.7	7.5	9.7	5.0	0.0			12.1
N	12	12	12	12	12	1			12

5-FEB-2004 18:55

Huntingdon Life Sciences 03-4254

PAGE186

APPENDIX H - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL BODY WEIGHT GAIN (GRAMS)									
FEMALES GROUP 4 400 MG/KG/DAY									
ANIMAL#	DAY OF STUDY								
	-5-0	0-6	6-13	13-20	20-27	27-34	34-41	41-48	0-27
4563	21	9	17	10	-1				35
4564	7	17	16	-3	11				41
4565	21	-2	24	15	0				37
4566	17	3	13	11	12				38
4567	18	16	1	23	-1				39
4568	23	15	25	14	17				71
4569	28	11	13	18	11				54
4570	26	21	1	23	-3				41
4571	21	-4	15	4	6				21
4572	19	-1	30	6	19				54
4573	19	17	2	29	9				57
4574	15	20	15	-1	17				52
MEAN	20	10	14	12	8				45
S.D.	5.4	9.0	9.4	9.7	7.9				13.1
N	12	12	12	12	12				12

5-FEB-2004 18:55

Huntingdon Life Sciences 03-4254

PAGE187

APPENDIX H - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

FEMALES GROUP 5 1000 MG/KG/DAY

INDIVIDUAL BODY WEIGHT GAIN (GRAMS)

ANIMAL#	DAY -5-0	OF 0-6	STUDY 6-13	13-20	20-27	27-34	34-41	41-48	0-27
5563	24	14	2	26	-1				40
5564	28	-1	26	16	4				44
5565	25	11	18	24	8				61
5566	30	5	9	16	15				44
5567	21	8	22	17	2				49
5568	40	4	13	21	16				55
5569	16	1	13	-6	16				23
5570	26	13	11	21	15				60
5571	11	6	13	10	13				43
5572	15	7	-5	16	-3				15
5573	12	17	11	18	20				65
5574	15	11	-2	19	7				36
MEAN	22	8	11	16	9				45
S.D.	8.4	5.4	9.2	8.2	7.5				15.0
N	12	12	12	12	12				12

5-FEB-2004 18:51

Huntingdon Life Sciences 03-4254

PAGE188

APPENDIX I - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL GESTATION BODY WEIGHTS (GRAMS)

GROUP 1 0 MG/KG/DAY

ANIMAL#	DAY OF GESTATION				
	0	7	14	17	20
1563	245	291	330	361	405
1564	272	308	349	373	426
1565	241	283	329	365	410
1566	279	312	357	389	443
1567x NP	221	290	294	289	311
1568	199	232	265	291	342
1569	255	285	310	341	393
1570	256	302	334	367	421
1571	268	293	333	357	407
1573	252	295	324	352	376
1574	269	309	343	366	396
MEAN	253	291	327	356	402
S.D.	22.8	23.1	25.4	26.1	28.0
N	10	10	10	10	10

NP=NOT PREGNANT x=EXCLUDED FROM MEAN

APPENDIX I - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL GESTATION BODY WEIGHTS (GRAMS)

GROUP 2 64 MG/KG/DAY

ANIMAL#	DAY OF GESTATION				
	0	7	14	17	20
2563	275	307	357	380	427
2564	274	323	359	388	425
2565	256	293	328	350	399
2566	209	243	274	298	332
2567	262	290	325	353	390
2568	248	277	314	330	378
2570	292	329	366	393	437
2571	268	309	352	382	430
2572x NP	269	301	311	301	294
2573	260	298	337	371	421
2574	245	289	326	349	383
MEAN	259	296	334	359	402
S.D.	22.4	24.6	27.3	29.7	32.4
N	10	10	10	10	10

NP=NOT PREGNANT x=EXCLUDED FROM MEAN

5-FEB-2004 18:51

Huntingdon Life Sciences 03-4254

PAGE190

APPENDIX I - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL GESTATION BODY WEIGHTS (GRAMS)

GROUP 3 160 MG/KG/DAY

ANIMAL#	DAY OF GESTATION				
	0	7	14	17	20
3563	258	300	339	372	425
3564	255	292	332	362	412
3565	250	291	312	341	388
3566	258	305	342	375	416
3567	228	258	283	314	364
3568	229	262	299	330	387
3569	249	275	297	312	333
3570	209	239	267	291	314
3571	278	325	362	394	445
3572	240	266	297	322	371
3573	272	321	358	394	429
3574	289	318	358	391	432
MEAN	251	288	320	350	393
S.D.	22.7	27.6	32.2	36.0	41.2
N	12	12	12	12	12

5-FEB-2004 18:51

Huntingdon Life Sciences 03-4254

PAGE191

APPENDIX I - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL GESTATION BODY WEIGHTS (GRAMS)

GROUP 4 400 MG/KG/DAY

ANIMAL#	DAY OF GESTATION				
	0	7	14	17	20
4563	247	290	332	362	399
4564	235	270	306	328	363
4565	258	292	327	359	417
4566	232	274	320	350	388
4567	244	282	326	351	400
4568	289	322	360	398	437
4569	271	301	338	366	411
4570	258	298	348	377	435
4571	204	238	276	301	333
4572	260	305	336	352	390
4573	265	318	374	405	445
4574	286	314	351	372	411
MEAN	254	292	333	360	402
S.D.	23.8	23.7	25.7	28.2	31.9
N	12	12	12	12	12

5-FEB-2004 18:51

Huntingdon Life Sciences 03-4254

PAGE192

APPENDIX I - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL GESTATION BODY WEIGHTS (GRAMS) .

GROUP 5 1000 MG/KG/DAY

ANIMAL#	DAY OF GESTATION				
	0	7	14	17	20
5563	242	276	309	338	375
5564	253	286	320	355	381
5565	273	307	340	372	406
5566	262	300	322	346	368
5567	264	270	311	335	373
5568	279	328	366	398	437
5569	229	260	299	321	365
5570	258	295	330	353	384
5571 TLL	234	258	298	319	353
5572x NP	218	219	228	232	222
5573	273	300	330	359	391
5574	240	270	302	318	337
MEAN	255	286	321	347	379
S.D.	17.0	21.8	20.4	24.6	26.7
N	11	11	11	11	11

NP=NOT PREGNANT TLL=TOTAL LITTER LOSS x=EXCLUDED FROM MEAN

5-FEB-2004 18:58

Huntingdon Life Sciences 03-4254

PAGE193

APPENDIX J - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL GESTATION BODY WEIGHT GAIN (GRAMS)

GROUP 1 0 MG/KG/DAY

ANIMAL#	DAY OF GESTATION				
	0 - 7	7 - 14	14 - 17	17 - 20	0 - 20
1563	46	39	32	44	160
1564	36	40	25	53	154
1565	42	46	36	46	169
1566	34	45	33	53	164
1567x NP	69	4	-5	21	89
1568	33	34	26	51	143
1569	30	25	31	52	138
1570	46	32	33	54	165
1571	25	40	25	50	139
1573	44	28	28	24	124
1574	40	34	23	30	127
MEAN	38	36	29	46	148
S.D.	7.3	6.8	4.3	10.3	16.3
N	10	10	10	10	10

NP=NOT PREGNANT

x=EXCLUDED FROM MEAN

APPENDIX J - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL GESTATION BODY WEIGHT GAIN (GRAMS)

GROUP 2 64 MG/KG/DAY

ANIMAL#	DAY OF GESTATION				
	0 - 7	7 - 14	14 - 17	17 - 20	0 - 20
2563	32	50	22	47	151
2564	49	37	29	37	151
2565	37	35	22	49	144
2566	34	32	23	35	124
2567	28	35	28	37	128
2568	29	36	17	48	130
2570	38	37	27	44	146
2571	41	43	30	48	161
2572x NP	32	11	-10	-7	25
2573	38	39	34	50	161
2574	45	36	24	34	138
MEAN	37	38	26	43	143
S.D.	6.6	5.1	4.9	6.5	13.3
N	10	10	10	10	10

NP=NOT PREGNANT

x=EXCLUDED FROM MEAN

5-FEB-2004 18:58

Huntingdon Life Sciences 03-4254

PAGE195

APPENDIX J - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL GESTATION BODY WEIGHT GAIN (GRAMS)

GROUP 3 160 MG/KG/DAY

ANIMAL#	DAY OF GESTATION				
	0 - 7	7 - 14	14 - 17	17 - 20	0 - 20
3563	42	39	33	53	167
3564	37	40	30	50	157
3565	41	22	29	47	138
3566	47	37	34	40	158
3567	30	25	31	50	136
3568	34	36	32	57	159
3569	26	22	15	21	83
3570	31	28	24	24	106
3571	47	37	31	51	167
3572	26	31	25	49	131
3573	49	37	36	35	157
3574	29	40	33	41	143
MEAN	36	33	29	43	142
S.D.	8.5	7.0	5.7	11.5	25.5
N	12	12	12	12	12

5-FEB-2004 18:58

Huntingdon Life Sciences 03-4254

PAGE196

APPENDIX J - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

GROUP 4 400 MG/KG/DAY INDIVIDUAL GESTATION BODY WEIGHT GAIN (GRAMS)

ANIMAL#	DAY OF GESTATION				
	0 - 7	7 - 14	14 - 17	17 - 20	0 - 20
4563	43	42	29	37	152
4564	35	36	22	35	128
4565	34	36	31	58	159
4566	42	46	30	38	155
4567	39	43	25	50	157
4568	33	38	38	39	148
4569	31	37	27	45	140
4570	39	50	29	57	176
4571	34	38	25	32	129
4572	45	31	16	38	129
4573	54	56	31	40	180
4574	28	37	21	40	125
MEAN	38	41	27	42	148
S.D.	7.2	7.0	5.9	8.4	18.5
N	12	12	12	12	12

5-FEB-2004 18:58

Huntingdon Life Sciences 03-4254

PAGE197

APPENDIX J - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL GESTATION BODY WEIGHT GAIN (GRAMS)

GROUP 5 1000 MG/KG/DAY

ANIMAL#	DAY OF GESTATION				
	0 - 7	7 - 14	14 - 17	17 - 20	0 - 20
5563	34	34	29	38	133
5564	33	34	35	27	128
5565	34	33	33	34	134
5566	38	22	25	22	106
5567	7	41	23	38	109
5568	50	38	32	39	158
5569	32	39	22	44	136
5570	36	36	23	31	125
5571 TLL	24	40	21	35	120
5572x NP	1	9	4	-10	5
5573	27	30	29	32	118
5574	31	31	17	19	97
MEAN	31	34	26	32	124
S.D.	10.5	5.5	5.8	7.6	16.8
N	11	11	11	11	11

NP=NOT PREGNANT TLL=TOTAL LITTER LOSS x=EXCLUDED FROM MEAN

Huntingdon Life Sciences 03-4254

APPENDIX K - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL MATERNAL LACTATION BODY WEIGHTS (GRAMS)

GROUP 1 0 MG/KG/DAY

Animal No.	DAY OF LACTATION					
	0 ^a	1	4	7	14	21
1563	318	303	311	336	349	364
1564	312	316	323	336	367	337
1565		315	318	331	353	335
1566	335	324	349	314	366	334
1567x NP						
1568	252	257	267	271	291	291
1569	280	289	315	330	333	327
1570	315	320	339	352	371	353
1571	312	304	328	326	346	327
1572	324	299	316	313	344	322
1573	279	277	308	313	338	326
1574		311	320	331	353	335
MEAN	303	301	318	323	347	332
S.D.	26.7	20.2	20.8	20.8	22.1	18.2
N	9	11	11	11	11	11

NP=NOT PREGNANT

x=EXCLUDED FROM MEAN

^aNo body weights were taken (missing values) for Day 0 females that were in process of delivery at the time body weights were recorded.

Huntingdon Life Sciences 03-4254

APPENDIX K - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL MATERNAL LACTATION BODY WEIGHTS (GRAMS)

GROUP 2 64 MG/KG/DAY

Animal No.	DAY OF LACTATION					
	0 ^a	1	4	7	14	21
2563	319	327	341	340	363	351
2564	343	333	346	363	389	378
2565	314	290	299	312	342	310
2566	.	243	261	268	288	274
2567	289	295	316	323	335	319
2568	289	274	308	312	347	332
2569	293	278	292	307	313	310
2570		332	344	364	381	366
2571	323	323	333	355	381	360
2572x NP						
2573	331	320	319	345	356	354
2574	313	300	309	326	331	315
MEAN	313	301	315	329	348	333
S.D.	19.0	28.7	25.8	28.8	30.7	30.9
N	9	11	11	11	11	11

NP=NOT PREGNANT

x=EXCLUDED FROM MEAN

^aNo body weights were taken (missing values) for Day 0 females that were in process of delivery at the time body weights were recorded.

Huntingdon Life Sciences 03-4254

APPENDIX K - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL MATERNAL LACTATION BODY WEIGHTS (GRAMS)

GROUP 3 160 MG/KG/DAY

Animal No.	DAY OF LACTATION					
	0 ^a	1	4	7	14	21
3563	301	312	324	329	345	334
3564	300	303	302	319	329	355
3565		292	314	315	340	353
3566	336	334	348	357	362	336
3567	258	268	270	278	311	289
3568	294	276	298	298	335	324
3569	288	285	286	294	304	298
3570	242	245	251	270	287	275
3571	323	326	351	353	367	344
3572	282	283	290	310	327	315
3573	339	327	348	354	369	349
3574	328	327	333	350	382	347
MEAN	299	298	310	319	338	326
S.D.	31.2	27.9	32.5	30.2	28.9	26.8
N	11	12	12	12	12	12

^aNo body weights were taken (missing values) for Day 0 females that were in process of delivery at the time body weights were recorded.

Huntingdon Life Sciences 03-4254

APPENDIX K - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL MATERNAL LACTATION BODY WEIGHTS (GRAMS)

GROUP 4 400 MG/KG/DAY

Animal No.	DAY OF LACTATION					
	0 ^a	1	4	7	14	21
4563	320	312	317	329	354	331
4564	266	258	254	280	302	295
4565	301	308	324	318	342	335
4566	283	280	301	306	325	312
4567	303	302	326	331	355	333
4568	337	324	349	364	388	364
4569		303	317	328	360	361
4570	318	317	333	340	359	354
4571	250	258	262	278	308	286
4572	314	309	343	349	372	344
4573	329	344	355	368	380	346
4574	326	310	327	352	381	351
MEAN	304	302	317	329	352	334
S.D.	27.4	25.4	31.5	29.2	28.1	25.1
N	11	12	12	12	12	12

^aNo body weights were taken (missing values) for Day 0 females that were in process of delivery at the time body weights were recorded.

Huntingdon Life Sciences 03-4254

APPENDIX K - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL MATERNAL LACTATION BODY WEIGHTS (GRAMS)

GROUP 5 1000 MG/KG/DAY

Animal No.	DAY OF LACTATION					
	0 ^a	1	4	7	14	21
5563	271	266	270	288	321	331
5564		281	288	303	331	338
5565		299	316	329	352	362
5566	283	291	299	322	359	359
5567	284	276	290	312	330	338
5568	346	334	356	383	405	390
5569	258	265	284	302	320	317
5570		272	291	316	355	372
5571 TLL	260	249				
5572x NP						
5573		290	291	308	285	339
5574	268	267	277	284	306	314
MEAN	282	281	296	315	336	346
S.D.	30.1	22.6	24.4	27.6	33.3	24.2
N	7	11	10	10	10	10

NP=NOT PREGNANT TLL=TOTAL LITTER LOSS x=EXCLUDED FROM MEAN

^aNo body weights were taken (missing values) for Day 0 females that were in process of delivery at the time body weights were recorded.

APPENDIX L - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL MATERNAL LACTATION BODY WEIGHT GAIN (GRAMS)

GROUP 1 0 MG/KG/DAY

FEMALE#	DAY OF LACTATION				
	1 - 4	4 - 7	7 - 14	14 - 21	1 - 21
1563	8	25	13	15	61
1564	8	13	32	-31	21
1565	3	14	22	-18	21
1566	25	-35	52	-33	9
1567x NP					
1568	9	5	20	0	34
1569	26	15	3	-6	38
1570	18	13	20	-18	33
1571	24	-2	20	-19	23
1572	17	-3	30	-21	24
1573	31	5	25	-12	49
1574	10	11	22	-19	24
MEAN	16	6	23	-15	31
S.D.	9.4	15.5	12.2	13.6	14.5
N	11	11	11	11	11

NP=NOT PREGNANT

x=EXCLUDED FROM MEAN

5-FEB-2004 19:09

Huntingdon Life Sciences 03-4254

PAGE 204

APPENDIX L - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL MATERNAL LACTATION BODY WEIGHT GAIN (GRAMS)

GROUP 2 64 MG/KG/DAY

FEMALE#	DAY OF LACTATION				
	1 - 4	4 - 7	7 - 14	14 - 21	1 - 21
2563	14	-1	23	-12	24
2564	13	17	26	-11	45
2565	9	13	30	-32	20
2566	18	7	20	-14	31
2567	21	8	11	-16	24
2568	33	4	36	-15	58
2569	14	15	6	-4	31
2570	12	20	18	-16	33
2571	10	22	26	-21	37
2572x NP					
2573	0	26	11	-2	35
2574	9	16	5	-16	15
MEAN	14	13	19	-14	32
S.D.	8.5	8.2	9.9	7.9	11.9
N	11	11	11	11	11

NP=NOT PREGNANT

x=EXCLUDED FROM MEAN

5-FEB-2004 19:09

Huntingdon Life Sciences 03-4254

PAGE 205

APPENDIX L - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL MATERNAL LACTATION BODY WEIGHT GAIN (GRAMS)

GROUP 3 160 MG/KG/DAY

FEMALE#	DAY OF LACTATION				
	1 - 4	4 - 7	7 - 14	14 - 21	1 - 21
3563	12	5	16	-11	23
3564	-1	17	10	26	52
3565	23	1	25	13	61
3566	14	9	5	-26	2
3567	2	8	32	-22	21
3568	23	0	37	-11	48
3569	0	9	9	-6	13
3570	6	20	17	-12	30
3571	25	2	14	-23	18
3572	7	19	17	-12	32
3573	21	6	15	-20	22
3574	7	16	33	-36	20
MEAN	11	9	19	-12	28
S.D.	9.4	7.2	10.2	17.0	17.4
N	12	12	12	12	12

5-FEB-2004 19:09

Huntingdon Life Sciences 03-4254

PAGE 206

APPENDIX L - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL MATERNAL LACTATION BODY WEIGHT GAIN (GRAMS)

GROUP 4 400 MG/KG/DAY

FEMALE#	DAY OF LACTATION				
	1 - 4	4 - 7	7 - 14	14 - 21	1 - 21
4563	5	12	24	-22	19
4564	-4	26	22	-8	37
4565	16	-6	24	-7	27
4566	21	5	20	-13	33
4567	24	5	24	-22	31
4568	25	15	24	-25	40
4569	14	11	32	2	59
4570	17	7	19	-5	37
4571	4	16	30	-22	28
4572	35	5	24	-28	35
4573	11	13	12	-34	2
4574	17	26	29	-30	41
MEAN	15	11	24	-18	32
S.D.	10.5	9.2	5.3	11.3	13.6
N	12	12	12	12	12

5-FEB-2004 19:09

Huntingdon Life Sciences 03-4254

PAGE 207

APPENDIX L - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL MATERNAL LACTATION BODY WEIGHT GAIN (GRAMS)

GROUP 5 1000 MG/KG/DAY

FEMALE#	DAY OF LACTATION				
	1 - 4	4 - 7	7 - 14	14 - 21	1 - 21
5563	4	18	33	10	65
5564	7	15	28	8	57
5565	17	13	24	9	63
5566	8	22	38	0	68
5567	14	22	18	8	62
5568	23	26	23	-15	57
5569	20	18	18	-3	52
5570	19	25	39	17	99
5571 TLL					
5572x NP					
5573	1	17	-22	54	50
5574	11	7	22	8	48
MEAN	12	18	22	10	62
S.D.	7.3	5.8	17.3	17.9	14.7
N	10	10	10	10	10

NP=NOT PREGNANT TLL=TOTAL LITTER LOSS x=EXCLUDED FROM MEAN

5-FEB-2004 19:07

Huntingdon Life Sciences 03-4254

PAGE 208

APPENDIX M - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

MALES GROUP 1 0 MG/KG/DAY INDIVIDUAL FEED CONSUMPTION (GRAMS/ANIMAL/DAY)

ANIMAL#	DAY OF STUDY						
	6	13	20	27	48	55	62
1063	26	25	25	24	24	25	25
1064	30	28	29	29	27	26	26
1065	23	22	23	24	25	27	28
1066	25	24	24	26	27	26	27
1067	26	26	27	28	28	27	30
1068	28	SF	26	26	28	28	29
1069	25	26	28	29	32	28	30
1070	24	23	23	23	25	24	25
1071	25	25	27	28	28	29	29
1072	26	27	30	30	30	29	29
1073	29	29	31	31	33	32	32
1074	26	25	27	25	26	25	26
MEAN	26	25	27	27	28	27	28
S.D.	2.0	2.1	2.7	2.6	2.6	2.0	2.2
N	12	11	12	12	12	12	12

SF=Spilled Feeder

5-FEB-2004 19:07

Huntingdon Life Sciences 03-4254

PAGE 209

APPENDIX M - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

MALES GROUP 2 64 MG/KG/DAY INDIVIDUAL FEED CONSUMPTION (GRAMS/ANIMAL/DAY)

ANIMAL#	DAY OF STUDY						
	6	13	20	27	48	55	62
2063	28	SF	30	SF	29	28	28
2064	25	SF	25	SF	26	26	26
2065	26	25	26	29	28	28	28
2066	25	24	25	25	25	23	25
2067	27	27	28	27	27	27	27
2068	27	27	28	29	28	28	27
2069	25	SF	25	SF	24	24	26
2070	27	27	29	28	28	27	28
2071	27	26	26	SF	26	26	27
2072	27	27	29	29	27	26	27
2073	31	32	32	32	31	31	31
2074	28	26	28	29	29	29	29
MEAN	27	27	28	28	27	27	28
S.D.	1.8	2.2	2.2	2.0	2.0	2.0	1.6
N	12	9	12	8	12	12	12

SF=Spilled Feeder

5-FEB-2004 19:07

Huntingdon Life Sciences 03-4254

PAGE 210

APPENDIX M - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

MALES GROUP 3 160 MG/KG/DAY INDIVIDUAL FEED CONSUMPTION (GRAMS/ANIMAL/DAY)

ANIMAL#	DAY OF STUDY						
	6	13	20	27	48	55	62
3063	26	26	28	30	SF	28	31
3064	25	24	25	27	27	25	26
3065	28	29	31	33	30	31	33
3066	26	25	26	28	28	26	27
3067	26	26	28	29	30	SF	30
3068	24	22	23	25	25	25	25
3069	22	21	23	25	25	26	26
3070	27	SF	20	27	26	25	25
3071	25	26	28	30	25	25	26
3072	27	24	26	23	24	25	26
3073	27	27	27	34	27	27	27
3074	29	SF	SF	23	30	29	29
MEAN	26	25	26	28	27	27	28
S.D.	2.0	2.3	3.1	3.5	2.2	2.1	2.5
N	12	10	11	12	11	11	12

SF=Spilled Feeder

5-FEB-2004 19:07

Huntingdon Life Sciences 03-4254

PAGE 211

APPENDIX M - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

MALES GROUP 4 400 MG/KG/DAY INDIVIDUAL FEED CONSUMPTION (GRAMS/ANIMAL/DAY)

ANIMAL#	DAY OF STUDY						
	6	13	20	27	48	55	62
4063	26	28	29	30	31	29	30
4064	27	26	28	27	24	27	27
4065	23	22	23	25	23	23	24
4066	29	27	29	30	30	27	29
4067	27	SF	28	26	29	29	29
4068	26	26	27	30	29	28	29
4069	26	26	28	28	28	27	28
4070	30	28	30	29	28	28	28
4071	28	29	30	32	30	31	32
4072	26	26	27	29	27	28	28
4073	27	26	26	28	27	26	27
4074	27	26	27	29	27	29	28
MEAN	27	26	28	29	28	28	28
S.D.	1.8	1.8	1.9	1.9	2.4	1.8	1.9
N	12	11	12	12	12	12	12

SF=Spilled Feeder

APPENDIX M - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

MALES GROUP 5 1000 MG/KG/DAY INDIVIDUAL FEED CONSUMPTION (GRAMS/ANIMAL/DAY)

ANIMAL#	DAY OF STUDY						
	6	13	20	27	48	55	62
5063	26	27	28	29	28	28	28
5064	26	27	30	29	31	30	31
5065	27	28	30	31	29	30	30
5066	27	25	24	24	26	25	27
5067	23	24	27	28	28	26	29
5068	24	26	29	30	30	32	30
5069	22	26	25	25	26	28	28
5070	25	SF	28	28	31	31	31
5071	24	23	26	26	27	26	25
5072	23	24	27	27	28	27	28
5073	24	23	26	27	25	26	26
5074	27	28	28	29	27	27	28
MEAN	25	26	27	28	28	28	28
S.D.	1.7	1.9	1.9	1.8	2.0	2.1	1.8
N	12	11	12	12	12	12	12

SF=Spilled Feeder

5-FEB-2004 19:07

Huntingdon Life Sciences 03-4254

PAGE 213

APPENDIX M - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

FEMALES GROUP 1 0 MG/KG/DAY
INDIVIDUAL FEED CONSUMPTION (GRAMS/ANIMAL/DAY)

ANIMAL#	DAY OF STUDY			
	6	13	20	27
1563	18	17	18	19
1564	19	21	18	17
1565	16	16	17	17
1566	19	19	18	18
1567	17	18	16	17
1568	15	15	16	15
1569	19	18	17	19
1570	18	16	29	SF
1571	SF	20	31	33
1572	20	18	19	19
1573	18	17	18	19
1574	19	18	18	19
MEAN	18	18	20	19
S.D.	1.5	1.8	4.9	4.6
N	11	12	12	11

SF=Spilled Feeder

5-FEB-2004 19:07

Huntingdon Life Sciences 03-4254

PAGE 214

APPENDIX M - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

FEMALES GROUP 2		64 MG/KG/DAY			
		INDIVIDUAL FEED CONSUMPTION (GRAMS/ANIMAL/DAY)			
ANIMAL#	DAY OF STUDY				
	6	13	20	27	
2563	19	19	20	20	
2564	24	SF	24	21	
2565	19	SF	20	SF	
2566	17	16	17	17	
2567	18	18	18	SF	
2568	18	17	17	17	
2569	CF	SF	20	21	
2570	24	SF	22	SF	
2571	20	19	19	18	
2572	22	25	19	18	
2573	19	SF	27	SF	
2574	21	23	16	15	
MEAN	20	20	20	18	
S.D.	2.4	3.3	3.2	2.2	
N	11	7	12	8	
SF=Spilled Feeder		CF=Contaminated Feeder			

5-FEB-2004 19:07

Huntingdon Life Sciences 03-4254

PAGE 215

APPENDIX M - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

FEMALES GROUP 3 160 MG/KG/DAY
INDIVIDUAL FEED CONSUMPTION (GRAMS/ANIMAL/DAY)

ANIMAL#	DAY OF STUDY			
	6	13	20	27
3563	18	17	19	19
3564	19	19	19	20
3565	18	17	17	17
3566	19	17	18	18
3567	18	17	18	18
3568	CF	CF	18	CF
3569	18	17	18	19
3570	16	15	16	17
3571	20	18	20	20
3572	19	19	20	18
3573	21	22	17	19
3574	20	20	20	SF
MEAN	19	18	18	18
S.D.	1.3	1.9	1.3	1.0
N	11	11	12	10

CF=Contaminated Feeder

SF=Spilled Feeder

5-FEB-2004 19:07

Huntingdon Life Sciences 03-4254

PAGE 216

APPENDIX M - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

FEMALES GROUP 4 400 MG/KG/DAY INDIVIDUAL FEED CONSUMPTION (GRAMS/ANIMAL/DAY)

ANIMAL#	DAY OF STUDY			
	6	13	20	27
4563	20	19	18	19
4564	18	18	17	18
4565	19	19	20	19
4566	18	16	17	17
4567	19	16	18	17
4568	20	20	20	22
4569	22	20	21	20
4570	20	19	18	17
4571	16	16	15	16
4572	19	21	20	22
4573	21	18	21	20
4574	22	20	20	20
MEAN	19	18	19	19
S.D.	1.7	1.7	1.8	1.8
N	12	12	12	12

5-FEB-2004 19:07

Huntingdon Life Sciences 03-4254

PAGE 217

APPENDIX M - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

FEMALES GROUP 5 1000 MG/KG/DAY
INDIVIDUAL FEED CONSUMPTION (GRAMS/ANIMAL/DAY)

ANIMAL#	DAY OF STUDY			
	6	13	20	27
5563	CF	CF	CF	18
5564	SF	18	20	20
5565	17	19	21	21
5566	18	20	20	22
5567	17	17	19	18
5568	21	20	23	22
5569	CF	CF	CF	CF
5570	17	18	20	20
5571	18	18	19	19
5572	18	17	19	17
5573	18	18	21	22
5574	18	17	19	18
MEAN	18	18	20	20
S.D.	1.1	0.9	1.4	1.8
N	9	10	10	11

CF=Contaminated Feeder

SF=Spilled Feeder

29-OCT-2003 12:22

PAGE 218

Huntingdon Life Sciences 03-4254

APPENDIX N - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL GESTATION FEED CONSUMPTION -- (GRAMS/ANIMAL/DAY)

GROUP 1 0 MG/KG/DAY

ANIMAL#	DAY OF GESTATION			
	0 - 7	7 - 14	14 - 20	0 - 20
1563	25	27	27	26
1564	24	25	24	25
1565	22	26	24	24
1566	24	25	26	25
1567x NP	24	23	18	22
1568	20	21	22	21
1569	21	22	23	22
1570	24	24	25	25
1571	22	24	24	23
1573	25	24	24	24
1574	24	25	22	24
MEAN	23	24	24	24
S.D.	1.8	2.0	1.6	1.6
N	10	10	10	10

NP=NOT PREGNANT

x=EXCLUDED FROM MEAN

Huntingdon Life Sciences 03-4254

APPENDIX N - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL GESTATION FEED CONSUMPTION -- (GRAMS/ANIMAL/DAY)

GROUP 2 64 MG/KG/DAY

ANIMAL#	DAY OF GESTATION			
	0 - 7	7 - 14	14 - 20	0 - 20
2563	25	28	CF	27
2564	23	26	26	25
2565	23	23	23	23
2566	20	21	22	21
2567	TE	24	23	23
2568	21	23	23	22
2570	27	27	26	27
2571	25	25	28	26
2572x NP	26	24	18	23
2573	24	CF	CF	24
2574	25	26	26	26
MEAN	24	25	25	24
S.D.	2.2	2.3	2.1	1.9
N	9	9	8	10

NP=NOT PREGNANT

x=EXCLUDED FROM MEAN

CF=Contaminated Feeder

TE=Technician Error: Food fed weight was not recorded.

Huntingdon Life Sciences 03-4254

APPENDIX N - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL GESTATION FEED CONSUMPTION -- (GRAMS/ANIMAL/DAY)

GROUP 3 160 MG/KG/DAY

ANIMAL#	DAY OF GESTATION			
	0 - 7	7 - 14	14 - 20	0 - 20
3563	25	27	26	26
3564	25	26	28	26
3565	21	23	23	23
3566	24	25	27	25
3567	22	22	23	23
3568	22	CF	25	23
3569	21	23	24	23
3570	18	21	19	19
3571	25	27	26	26
3572	21	22	23	22
3573	25	27	26	26
3574	24	27	27	26
MEAN	23	25	25	24
S.D.	2.2	2.4	2.4	2.3
N	12	11	12	12

CF=Contaminated Feeder

Huntingdon Life Sciences 03-4254

APPENDIX N - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL GESTATION FEED CONSUMPTION -- (GRAMS/ANIMAL/DAY)

GROUP 4 400 MG/KG/DAY

ANIMAL#	DAY OF GESTATION			
	0 - 7	7 - 14	14 - 20	0 - 20
4563	23	26	24	25
4564	22	23	22	22
4565	23	24	26	24
4566	23	25	CF	24
4567	22	25	26	24
4568	24	26	28	26
4569	24	24	25	25
4570	22	24	CF	23
4571	20	21	23	21
4572	23	25	24	24
4573	28	32	31	30
4574	TE	26	26	26
MEAN	23	25	26	25
S.D.	2.0	2.5	2.5	2.2
N	11	12	10	12

CF=Contaminated Feeder

TE=Technician Error: Food fed weight was not recorded.

Huntingdon Life Sciences 03-4254

APPENDIX N - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL GESTATION FEED CONSUMPTION -- (GRAMS/ANIMAL/DAY)

GROUP 5 1000 MG/KG/DAY

ANIMAL#	DAY OF GESTATION			
	0 - 7	7 - 14	14 - 20	0 - 20
5563	CF	CF	CF	CF
5564	23	24	24	24
5565	TE	25	25	25
5566	24	20	24	23
5567	TE	24	24	24
5568	28	30	31	30
5569	20	23	CF	22
5570	22	23	24	23
5571 TLL	19	21	20	20
5572x NP	TE	18	15	17
5573	23	24	25	24
5574	23	23	24	23
MEAN	23	24	25	24
S.D.	2.7	2.8	2.9	2.6
N	8	10	9	10

NP=NOT PREGNANT TLL=TOTAL LITTER LOSS x=EXCLUDED FROM MEAN

CF=Contaminated Feeder TE=Technician Error: Food fed weight was not recorded.

Huntingdon Life Sciences 03-4254

APPENDIX O - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL MATERNAL LACTATION FEED CONSUMPTION -- (GRAMS/ANIMAL/DAY)

GROUP 1 0 MG/KG/DAY

ANIMAL#	DAY OF LACTATION			
	1 - 4	4 - 7	7 - 14	1 - 14
1563	37	48	61	49
1564	33	46	61	47
1565	32	44	62	46
1566	38	EF	66	52
1567x NP				
1568	40	45	59	48
1569	41	49	61	51
1570	47	55	69	57
1571	39	EF	64	51
1572	27	36	52	38
1573	41	49	66	52
1574	36	EF	64	50
MEAN	37	46	62	49
S.D.	5.3	5.4	4.5	4.7
N	11	8	11	11

NP=NOT PREGNANT

x=EXCLUDED FROM MEAN

EF=Empty Feeder

CF=Contaminated Feeder

Huntingdon Life Sciences 03-4254

APPENDIX O - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL MATERNAL LACTATION FEED CONSUMPTION -- (GRAMS/ANIMAL/DAY)

GROUP 2 64 MG/KG/DAY

ANIMAL#	DAY OF LACTATION			
	1 - 4	4 - 7	7 - 14	1 - 14
2563	41	51	67	53
2564	39	52	64	51
2565	32	47	62	47
2566	31	37	50	39
2567	33	47	56	46
2568	40	49	63	50
2569	31	45	60	45
2570	35	46	64	48
2571	40	CF	77	59
2572x NP				
2573	33	51	63	49
2574	27	41	44	38
MEAN	35	47	61	48
S.D.	4.6	4.7	8.6	5.9
N	11	10	11	11

NP=NOT PREGNANT x=EXCLUDED FROM MEAN

CF=Contaminated Feeder

Huntingdon Life Sciences 03-4254

APPENDIX O - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL MATERNAL LACTATION FEED CONSUMPTION -- (GRAMS/ANIMAL/DAY)

GROUP 3 160 MG/KG/DAY

ANIMAL#	DAY OF LACTATION			
	1 - 4	4 - 7	7 - 14	1 - 14
3563	42	48	EF	45
3564	35	47	55	46
3565	34	EF	62	48
3566	39	48	54	47
3567	42	45	62	50
3568	30	46	59	45
3569	17	27	30	25
3570	23	42	52	39
3571	42	55	EF	49
3572	36	50	62	49
3573	41	CF	66	54
3574	42	54	68	55
MEAN	35	46	57	46
S.D.	8.2	7.8	10.9	7.9
N	12	10	10	12

EF=Empty Feeder

CF=Contaminated Feeder

29-OCT-2003 12:09

PAGE 226

Huntingdon Life Sciences 03-4254

APPENDIX O - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL MATERNAL LACTATION FEED CONSUMPTION -- (GRAMS/ANIMAL/DAY)

GROUP 4 400 MG/KG/DAY

ANIMAL#	DAY OF LACTATION			
	1 - 4	4 - 7	7 - 14	1 - 14
4563	34	45	61	47
4564	15	41	54	37
4565	37	47	57	47
4566	36	49	61	49
4567	39	49	60	49
4568	48	54	67	56
4569	35	48	62	48
4570	38	49	CF	43
4571	30	45	57	44
4572	42	54	67	54
4573	42	60	69	57
4574	34	55	66	52
MEAN	36	50	62	49
S.D.	8.1	5.2	4.9	5.8
N	12	12	11	12

CF=Contaminated Feeder

Huntingdon Life Sciences 03-4254

APPENDIX O - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL MATERNAL LACTATION FEED CONSUMPTION -- (GRAMS/ANIMAL/DAY)

GROUP 5 1000 MG/KG/DAY

ANIMAL#	DAY OF LACTATION			
	1 - 4	4 - 7	7 - 14	1 - 14
5563	16	34	46	32
5564	37	58	54	50
5565	27	38	56	40
5566	33	45	55	44
5567	31	44	54	43
5568	38	53	64	51
5569	36	51	61	49
5570	26	44	57	42
5571 TLL				
5572x NP				
5573	20	29	28	26
5574	27	36	43	35
MEAN	29	43	52	41
S.D.	7.2	9.1	10.3	8.2
N	10	10	10	10

NP=NOT PREGNANT

TLL=TOTAL LITTER LOSS

x=EXCLUDED FROM MEAN

APPENDIX P - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENT TOXICITY SCREENING IN RATS

INDIVIDUAL MATING/ESTROUS CYCLE DATA

GROUP 1 0 MG/KG/DAY

FEMALE#	DAY OF MATING														NE
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
1563	S														0
1564	D	P	E	D	D	D	C								1
1565	D	C													0
1566	D	P	S												0
1567	S														0
1568	S														0
1569	E	C													0
1570	C														0
1571	E	E	S												0
1572	D	D	/P	D	D	D	D	D	D	D	D	D	D	D	0
1573	C														0
1574	D	D	C												0

D=DIESTRUS M=METESTRUS P=PROESTRUS E=ESTRUS S=SPERM C=COPULATORY PLUG /=PRESUMED MATING DAY NE=NUMBER OF ESTROUS STAGES
PASSED WITHOUT MATING

28-Oct-03

Page 229

Huntingdon Life Sciences 03-4254

APPENDIX P - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENT TOXICITY SCREENING IN RATS

INDIVIDUAL MATING/ESTROUS CYCLE DATA

GROUP 2 64 MG/KG/DAY

FEMALE#	DAY OF MATING														NE
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
2563	D	S													0
2564	E	D	D	D	P	S									1
2565	S														0
2566	S														0
2567	D	D	D	S											0
2568	D	D	P	S											0
2569	D	D	/E	M	D	D	D	D	D	D	D	D	D	D	0
2570	S														0
2571	D	E	C												0
2572	D	D	C												0
2573	E	C													0
2574	E	E	S												0

D=DIESTRUS M=METESTRUS P=PROESTRUS E=ESTRUS S=SPERM C=COPULATORY PLUG /=PRESUMED MATING DAY NE=NUMBER OF ESTROUS STAGES
 PASSED WITHOUT MATING

APPENDIX P - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENT TOXICITY SCREENING IN RATS

INDIVIDUAL MATING/ESTROUS CYCLE DATA

GROUP 3 160 MG/KG/DAY

FEMALE#	DAY OF MATING														NE
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
3563	D	C													0
3564	C														0
3565	D	D	D	E	E	D	D	D	E	S					1
3566	D	D	D	E	S										0
3567	C														0
3568	D	S													0
3569	C														0
3570	D	D	E	S											0
3571	D	D	C												0
3572	E	C													0
3573	D	D	D	E	S										0
3574	S														0

D=DIESTRUS E=ESTRUS S=SPERM C=COPULATORY PLUG NE=NUMBER OF ESTROUS STAGES PASSED WITHOUT MATING

APPENDIX P - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENT TOXICITY SCREENING IN RATS

INDIVIDUAL MATING/ESTROUS CYCLE DATA

GROUP 4 400 MG/KG/DAY

FEMALE#	DAY OF MATING														NE
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
4563	D	D	C												0
4564	D	D	D	C											0
4565	D	D	C												0
4566	D	E	C												0
4567	D	D	C												0
4568	D	D	D	P	C										0
4569	D	S													0
4570	D	D	C												0
4571	D	E	S												0
4572	D	D	E	S											0
4573	D	S													0
4574	D	D	E	S											0

D=DIESTRUS P=PROESTRUS E=ESTRUS S=SPERM C=COPULATORY PLUG NE=NUMBER OF ESTROUS STAGES PASSED WITHOUT MATING

APPENDIX P - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENT TOXICITY SCREENING IN RATS

INDIVIDUAL MATING/ESTROUS CYCLE DATA

GROUP 5 1000 MG/KG/DAY

FEMALE#	DAY OF MATING														NE
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
5563	D	D	C												0
5564	D	S													0
5565	D	D	D	P	S										0
5566	D	D	D	E	S										0
5567	D	D	D	S											0
5568	E	S													0
5569	D	D	C												0
5570	C														0
5571	D	P	S												0
5572	E	E	D	E	S										1
5573	D	D	D	C											0
5574	C														0

D=DIESTRUS P=PROESTRUS E=ESTRUS S=SPERM C=COPULATORY PLUG NE=NUMBER OF ESTROUS STAGES PASSED WITHOUT MATING

6-FEB-2004 10:00

Huntingdon Life Sciences 03-4254

PAGE 233

APPENDIX Q - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL MATING ASSIGNMENTS

GROUP 1 0 MG/KG/DAY

Female No.	Male No.	Sperm/Plug	Outcome	Date of Cohabitation	Date of Insemination
1563	1063	+	P	15-JUL-03	16-JUL-03
1564	1064	+	P	15-JUL-03	22-JUL-03
1565	1065	+	P	15-JUL-03	17-JUL-03
1566	1066	+	P	15-JUL-03	18-JUL-03
1567	1067	+	NP	15-JUL-03	16-JUL-03
1568	1068	+	P	15-JUL-03	16-JUL-03
1569	1069	+	P	15-JUL-03	17-JUL-03
1570	1070	+	P	15-JUL-03	16-JUL-03
1571	1071	+	P	15-JUL-03	18-JUL-03
1572	1072	-	P	15-JUL-03	
1573	1073	+	P	15-JUL-03	16-JUL-03
1574	1074	+	P	15-JUL-03	18-JUL-03

+ = Sperm/Plug Positive - = Sperm/Plug Negative

NP=NOT PREGNANT P=PREGNANT

6-FEB-2004 10:00

Huntingdon Life Sciences 03-4254

PAGE 234

APPENDIX Q - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL MATING ASSIGNMENTS

GROUP 2 64 MG/KG/DAY

Female No.	Male No.	Sperm/Plug	Outcome	Date of Cohabitation	Date of Insemination
2563	2063	+	P	15-JUL-03	17-JUL-03
2564	2064	+	P	15-JUL-03	21-JUL-03
2565	2065	+	P	15-JUL-03	16-JUL-03
2566	2066	+	P	15-JUL-03	16-JUL-03
2567	2067	+	P	15-JUL-03	19-JUL-03
2568	2068	+	P	15-JUL-03	19-JUL-03
2569	2069	-	P	15-JUL-03	
2570	2070	+	P	15-JUL-03	16-JUL-03
2571	2071	+	P	15-JUL-03	18-JUL-03
2572	2072	+	NP	15-JUL-03	18-JUL-03
2573	2073	+	P	15-JUL-03	17-JUL-03
2574	2074	+	P	15-JUL-03	18-JUL-03

+ = Sperm/Plug Positive - = Sperm/Plug Negative

NP=NOT PREGNANT

P=PREGNANT

6-FEB-2004 10:00

Huntingdon Life Sciences 03-4254

PAGE 235

APPENDIX Q - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL MATING ASSIGNMENTS

GROUP 3 160 MG/KG/DAY

Female No.	Male No.	Sperm/Plug	Outcome	Date of Cohabitation	Date of Insemination
3563	3063	+	P	15-JUL-03	17-JUL-03
3564	3064	+	P	15-JUL-03	16-JUL-03
3565	3065	+	P	15-JUL-03	25-JUL-03
3566	3066	+	P	15-JUL-03	20-JUL-03
3567	3067	+	P	15-JUL-03	16-JUL-03
3568	3068	+	P	15-JUL-03	17-JUL-03
3569	3069	+	P	15-JUL-03	16-JUL-03
3570	3070	+	P	15-JUL-03	19-JUL-03
3571	3071	+	P	15-JUL-03	18-JUL-03
3572	3072	+	P	15-JUL-03	17-JUL-03
3573	3073	+	P	15-JUL-03	20-JUL-03
3574	3074	+	P	15-JUL-03	16-JUL-03

+ = Sperm/Plug Positive - = Sperm/Plug Negative

P=PREGNANT

6-FEB-2004 10:00

Huntingdon Life Sciences 03-4254

PAGE 236

APPENDIX Q - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL MATING ASSIGNMENTS

GROUP 4 400 MG/KG/DAY

Female No.	Male No.	Sperm/Plug	Outcome	Date of Cohabitation	Date of Insemination
4563	4063	+	P	15-JUL-03	18-JUL-03
4564	4064	+	P	15-JUL-03	19-JUL-03
4565	4065	+	P	15-JUL-03	18-JUL-03
4566	4066	+	P	15-JUL-03	18-JUL-03
4567	4067	+	P	15-JUL-03	18-JUL-03
4568	4068	+	P	15-JUL-03	20-JUL-03
4569	4069	+	P	15-JUL-03	17-JUL-03
4570	4070	+	P	15-JUL-03	18-JUL-03
4571	4071	+	P	15-JUL-03	18-JUL-03
4572	4072	+	P	15-JUL-03	19-JUL-03
4573	4073	+	P	15-JUL-03	17-JUL-03
4574	4074	+	P	15-JUL-03	19-JUL-03

+ = Sperm/Plug Positive - = Sperm/Plug Negative

P=PREGNANT

6-FEB-2004 10:00

Huntingdon Life Sciences 03-4254

PAGE 237

APPENDIX Q - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL MATING ASSIGNMENTS

GROUP 5 1000 MG/KG/DAY

Female No.	Male No.	Sperm/Plug	Outcome	Date of Cohabitation	Date of Insemination
5563	5063	+	P	15-JUL-03	18-JUL-03
5564	5064	+	P	15-JUL-03	17-JUL-03
5565	5066	+	P	15-JUL-03	20-JUL-03
5566	5065	+	P	15-JUL-03	20-JUL-03
5567	5067	+	P	15-JUL-03	19-JUL-03
5568	5068	+	P	15-JUL-03	17-JUL-03
5569	5069	+	P	15-JUL-03	18-JUL-03
5570	5070	+	P	15-JUL-03	16-JUL-03
5571	5071	+	TLL	15-JUL-03	18-JUL-03
5572	5072	+	NP	15-JUL-03	20-JUL-03
5573	5073	+	P	15-JUL-03	19-JUL-03
5574	5074	+	P	15-JUL-03	16-JUL-03

+ = Sperm/Plug Positive - = Sperm/Plug Negative

NP=NOT PREGNANT TLL=TOTAL LITTER LOSS P=PREGNANT

	Individual Litter and Delivery Data F ₀ Generation	Appendix R
--	--	------------

Abbreviations:

no day 0 = no day 0 pre-coitus

Note:

The uteri of animals 2566 (13 pups) and 2570 (14 pups) were not examined for implantation scars.

APPENDIX R - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL DELIVERY AND LITTER DATA

GROUP 1 0 MG/KG/DAY

		LITTER DELIVERED			NUMBER OF LIVE PUPS												TOTAL IMPLAN- TATIONS N	DURATION OF GESTATION (DAYS) N
		LIVE N	DEAD N	TOTAL N	DAYS													
FEMALE#					1		4		4		7		14		21			
					M	F	M	F	M	F	M	F	M	F				
	1563	14	0	14	7	7	7	7	5	5	5	5	5	5	15	22		
	1564	16	1	17	10	6	9	6	5	5	5	5	5	5	19	22		
	1565	16	0	16	8	8	7	8	5	5	5	5	5	5	16	21		
	1566	18	1	19	12	6	12	6	5	5	5	5	5	5	19	22		
	1567x NP																	
	1568	14	0	14	8	6	8	6	5	5	5	5	5	5	14	22		
	1569	16	0	16	5	10	5	10	5	5	5	5	5	5	17	22		
	1570	16	0	16	10	6	10	6	5	5	5	5	5	5	16	22		
	1571	15	1	16	10	5	10	5	5	5	5	5	5	5	17	22		
	1572	15	0	15	7	8	7	8	5	5	5	5	5	5	15	no day 0 pc		
	1573	15	0	15	7	7	7	7	5	5	5	5	5	5	16			
	1574	14	0	14	7	7	7	5	5	5	5	5	5	5	15	22		
MEAN		15.4	0.3	15.6	8.3	6.9	8.1	6.7	5.0	5.0	5.0	5.0	5.0	5.0	16.3	21.9		
S.D.		1.2	0.5	1.5	2.0	1.4	2.0	1.5	0.0	0.0	0.0	0.0	0.0	0.0	1.6	0.3		
N		11	11	11	11	11	11	11	11	11	11	11	11	11	11	10		

NP=NOT PREGNANT

x=EXCLUDED FROM MEAN

DAY 4 COLUMNS = PRE- AND POSTCULLING RESPECTIVELY

APPENDIX R - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL DELIVERY AND LITTER DATA

GROUP 2 64 MG/KG/DAY

LITTER DELIVERED				NUMBER OF LIVE PUPS												TOTAL IMPLAN- TATIONS N	DURATION OF GESTATION (DAYS) N
FEMALE#	LIVE N	DEAD N	TOTAL N	DAYS													
				1		4		4		7		14		21			
				M	F	M	F	M	F	M	F	M	F	M	F		
2563	16	0	16	6	10	6	10	5	5	5	5	5	5	5	5	16	22
2564	13	0	13	4	9	4	9	4	6	4	6	4	6	4	6	14	22
2565	15	0	15	10	5	10	5	5	5	5	5	5	5	5	5	16	22
2566	13	0	13	6	7	6	7	5	5	5	5	5	5	5	5		21
2567	13	0	13	8	5	8	4	6	4	6	4	6	4	6	4	15	22
2568	14	1	15	9	4	9	4	6	4	6	4	6	4	6	4	16	22
2569	15	0	15	6	9	6	9	5	5	5	5	5	5	5	5	16	no day 0 pc
2570	14	0	14	7	7	7	7	5	5	5	5	5	5	5	5		21
2571	16	0	16	9	7	9	7	5	5	5	5	5	5	5	5	19	23
2572x NP																	
2573	15	0	15	10	5	10	5	5	5	5	5	5	5	5	5	15	22
2574	9	0	9	4	5	4	5	4	5	4	5	4	5	4	5	9	22
MEAN	13.9	0.1	14.0	7.2	6.6	7.2	6.5	5.0	4.9	5.0	4.9	5.0	4.9	5.0	4.9	15.1	21.9
S.D.	2.0	0.3	2.0	2.2	2.0	2.2	2.1	0.6	0.5	0.6	0.5	0.6	0.5	0.6	0.5	2.7	0.6
N	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	9	10

NP=NOT PREGNANT

x=EXCLUDED FROM MEAN

DAY 4 COLUMNS = PRE- AND POSTCULLING RESPECTIVELY

APPENDIX R - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL DELIVERY AND LITTER DATA

GROUP 3 160 MG/KG/DAY

FEMALE#	LITTER DELIVERED			NUMBER OF LIVE PUPS												TOTAL IMPLAN- TATIONS N	DURATION OF GESTATION (DAYS) N
	LIVE N	DEAD N	TOTAL N	DAYS													
				1		4		4		7		14		21			
				M	F	M	F	M	F	M	F	M	F	M	F		
3563	19	0	19	11	7	11	7	5	5	5	5	5	5	5	5	19	22
3564	15	0	15	6	9	6	9	5	5	5	5	5	5	5	5	15	22
3565	15	0	15	6	9	6	9	5	5	5	5	5	5	5	5	17	21
3566	14	0	14	11	3	11	3	7	3	7	3	7	3	7	3	16	22
3567	16	0	16	6	10	6	10	5	5	5	5	5	5	5	5	16	22
3568	14	0	14	9	5	9	5	5	5	5	5	5	5	5	5	15	22
3569	2	3	5	0	2	0	2	0	2	0	2	0	2	0	2	5	24
3570	11	0	11	5	6	5	6	5	5	5	5	5	5	5	5	14	22
3571	14	1	15	6	8	6	8	5	5	5	5	5	5	5	5	18	23
3572	15	0	15	9	6	9	6	5	5	5	5	5	5	5	5	17	22
3573	16	0	16	6	9	6	9	5	5	5	5	5	5	5	5	17	22
3574	14	0	14	7	6	7	6	5	5	5	5	5	5	5	5	14	22
MEAN	13.8	0.3	14.1	6.8	6.7	6.8	6.7	4.8	4.6	4.8	4.6	4.8	4.6	4.8	4.6	15.3	22.2
S.D.	4.1	0.9	3.4	3.0	2.5	3.0	2.5	1.6	1.0	1.6	1.0	1.6	1.0	1.6	1.0	3.6	0.7
N	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12

DAY 4 COLUMNS = PRE- AND POSTCULLING RESPECTIVELY

6-FEB-2004 16:28

Huntingdon Life Sciences 03-4254

PAGE242

APPENDIX R - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL DELIVERY AND LITTER DATA

GROUP 4 400 MG/KG/DAY

FEMALE#	LITTER DELIVERED			NUMBER OF LIVE PUPS												TOTAL IMPLAN- TATIONS N	DURATION OF GESTATION (DAYS) N
	LIVE N	DEAD N	TOTAL N	DAYS													
				1		4		4		7		14		21			
				M	F	M	F	M	F	M	F	M	F	M	F		
4563	13	0	13	7	6	7	6	5	5	5	5	5	5	5	5	17	21
4564	15	0	15	8	7	8	7	5	5	5	5	5	5	5	5	16	22
4565	18	0	18	11	6	11	6	5	5	5	5	5	5	5	5	18	22
4566	14	0	14	7	7	7	7	5	5	5	5	4	5	4	5	17	23
4567	15	0	15	9	6	9	6	5	5	5	5	5	5	5	5	15	23
4568	16	0	16	9	7	9	7	5	5	5	5	5	5	5	5	18	22
4569	11	3	14	6	5	6	5	5	5	5	5	5	5	5	5	16	22
4570	18	0	18	7	11	7	11	5	5	5	5	5	5	5	5	18	23
4571	10	0	10	6	4	6	4	6	4	6	4	6	4	6	4	14	23
4572	13	0	13	5	8	5	8	5	5	5	5	5	5	5	5	15	22
4573	15	0	15	10	5	10	5	5	5	5	5	5	5	5	5	15	23
4574	12	1	13	5	7	5	7	5	5	5	5	5	5	5	5	14	22
MEAN	14.2	0.3	14.5	7.5	6.6	7.5	6.6	5.1	4.9	5.1	4.9	5.0	4.9	5.0	4.9	16.1	22.3
S.D.	2.5	0.9	2.2	1.9	1.8	1.9	1.8	0.3	0.3	0.3	0.3	0.4	0.3	0.4	0.3	1.5	0.7
N	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12

DAY 4 COLUMNS = PRE- AND POSTCULLING RESPECTIVELY

APPENDIX R - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL DELIVERY AND LITTER DATA

GROUP 5 1000 MG/KG/DAY

LITTER DELIVERED				NUMBER OF LIVE PUPS												TOTAL IMPLAN- TATIONS N	DURATION OF GESTATION (DAYS) N	
FEMALE#	LIVE N	DEAD N	TOTAL N	DAYS														
				1		4		4		7		14		21				
				M	F	M	F	M	F	M	F	M	F	M	F			
5563		11	3	14	1	5	0	5	0	5	0	5	0	5	0	5	17	23
5564		13	1	14	6	7	6	7	5	5	5	5	5	5	5	5	17	22
5565		17	0	17	9	8	9	7	5	5	5	5	5	5	5	5	17	22
5566		14	0	14	7	7	7	7	5	5	5	5	5	5	5	5	15	23
5567		16	0	16	8	8	8	8	5	5	5	5	5	5	5	5	18	22
5568		14	0	14	7	6	7	6	5	5	5	5	5	5	5	5	15	23
5569		13	0	13	7	5	7	5	5	5	5	5	5	5	5	5	15	23
5570		11	1	12	5	4	5	4	5	4	5	4	5	4	5	4	15	22
5571	TLL	15	1	16	1	0	0	0	0	0	0	0	0	0	0	0	16	23
5572x	NP																	
5573		15	0	15	6	0	6	0	6	0	5	0	5	0	5	0	16	22
5574		8	0	8	3	2	3	2	3	2	3	2	3	2	3	2	16	23
MEAN		13.4	0.5	13.9	5.5	4.7	5.8	5.1	4.4	4.1	4.3	4.1	4.3	4.1	4.3	4.1	16.1	22.5
S.D.		2.6	0.9	2.4	2.7	2.9	2.6	2.5	1.7	1.7	1.6	1.7	1.6	1.7	1.6	1.7	1.0	0.5
N		11	11	11	11	11	10	10	10	10	10	10	10	10	10	10	11	11

NP=NOT PREGNANT TLL=TOTAL LITTER LOSS x=EXCLUDED FROM MEAN

DAY 4 COLUMNS = PRE- AND POSTCULLING RESPECTIVELY

APPENDIX S - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP SEX AND STATUS DURING LACTATION

GROUP 1 0 MG/KG/DAY

FEMALE#	PUP #																						
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
1563	MC 4	MK21	MK21	MC 4	MK23	MK21	MP21	FP21	FK23	FK21	FC 4	FK21	FC 4	FK21									
1564	MS	MC 4	MC 4	MK21	MK21	MK21	MK23	MC 4	MC 4	MD 3	MP21	FK21	FC 4	FK21	FK21	FK23	FP21						
1565	MM 2	MP21	MK21	MC 4	MC 4	MK21	MK23	MK21	FK23	FK21	FC 4	FK21	FC 4	FC 4	FK21	FP21							
1566	FS	MK21	MC 4	MC 4	MK23	MK21	MC 4	MC 4	MC 4	MC 4	MC 4	MK21	MP21	FK23	FK21	FK21	FC 4	FK21	FP21				
1568	MC 4	MC 4	MP21	MK23	MK21	MK21	MK21	MC 4	FP21	FK23	FK21	FC 4	FK21	FK21									
1569	MD 0	MK21	MK21	MK21	MK23	MP21	FK23	FC 4	FC 4	FC 4	FC 4	FK21	FK21	FK21	FC 4	FP21							
1570	MC 4	MC 4	MP21	MK23	MK21	MC 4	MK21	MC 4	MC 4	MK21	FC 4	FK23	FP21	FK21	FK21	FK21							
1571	FS	MC 4	MK21	MK21	MC 4	MK21	MC 4	MC 4	MP21	MK23	MC 4	FK21	FK21	FK21	FK23	FP21							
1572	MP21	MK23	MK21	MC 4	MK21	MC 4	MK21	FK21	FK21	FC 4	FK21	FP21	FC 4	FK23	FC 4								
1573	FD 0	MK23	MC 4	MK21	MK21	MK21	MC 4	MP21	FC 4	FC 4	FK21	FK23	FP21	FK21	FK21								
1574	MP21	MK21	MC 4	MK21	MK21	MC 4	MK23	FK21	FK21	FK21	FK23	FP21	FM 2	FM 2									

SEX CODE PRECEDES PUP STATUS CODE. NUMERICAL VALUE INDICATES DAY OF LACTATION.

SEX CODES: M-MALE F-FEMALE U-UNCERTAIN

PUP STATUS CODES: A-ALIVE S-STILLBORN D-DIED C-CULLED M-MISSING K-SCHEDULED SACRIFICE P-SELECTED PARENT

APPENDIX S - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP SEX AND STATUS DURING LACTATION.

GROUP 2 64 MG/KG/DAY

FEMALE#	PUP #																						
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
2563	MK21	MK21	MC 4	MK23	MK21	MP21	FC 4	FC 4	FP21	FC 4	FK21	FK21	FK21	FC 4	FC 4	FK23							
2564	MK21	MK21	MP21	MK23	FP21	FK21	FK23	FC 4	FC 4	FK21	FC 4	FK21	FK21										
2565	MK21	MK21	MK21	MC 4	MK23	MC 4	MC 4	MC 4	MC 4	MP21	FK21	FK21	FK21	FK23	FP21								
2566	MK23	MK21	MP21	MK21	MC 4	MK21	FK21	FC 4	FC 4	FK21	FK21	FP21	FK23										
2567	MC 4	MK21	MK21	MP21	MK23	MK21	MK21	MC 4	FK21	FK23	FK21	FP21	FD 2										
2568	MD 0	MS	MP21	MK23	MK21	MK21	MK21	MC 4	MC 4	MC 4	FK21	FK23	FK21	FP21									
2569	MC 4	MK21	MP21	MK21	MK21	MK23	FP21	FK21	FC 4	FC 4	FK21	FK21	FC 4	FK23									
2570	MK21	MK21	MP21	MK21	MK23	MC 4	MC 4	FK21	FK21	FK21	FK23	FC 4	FC 4	FP21									
2571	MP21	MC 4	MK21	MC 4	MC 4	MC 4	MK21	MK21	MK23	FK21	FK23	FC 4	FP21	FK21	FC 4	FK21							
2573	MC 4	MC 4	MC 4	MK21	MK21	MK21	MC 4	MK23	MC 4	MP21	FK21	FK23	FK21	FK21	FP21								
2574	MP21	MK23	MK21	MK21	FK21	FK21	FP21	FK21	FK23														

SEX CODE PRECEDES PUP STATUS CODE. NUMERICAL VALUE INDICATES DAY OF LACTATION.

SEX CODES: M-MALE F-FEMALE U-UNCERTAIN

PUP STATUS CODES: A-ALIVE S-STILLBORN D-DIED C-CULLED K-SCHEDULED SACRIFICE P-SELECTED PARENT

APPENDIX S - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP SEX AND STATUS DURING LACTATION

GROUP 3 160 MG/KG/DAY

FEMALE#	PUP #																						
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
3563	MC 4	MK21	MC 4	MC 4	MK21	MP21	MK21	MD 1	MK23	MC 4	MC 4	FK21	FP21	FC 4	MC 4	FC 4	FK21	FK21	FK23				
3564	MC 4	MK21	MK21	MK21	MK23	MP21	FC 4	FK21	FK23	FK21	FP21	FK21	FC 4	FC 4	FC 4								
3565	MK21	MK21	MP21	MK23	MC 4	MK21	FC 4	FC 4	FK23	FP21	FC 4	FK21	FK21	FK21	FC 4								
3566	MC 4	MK21	MK21	MP21	MC 4	MK23	MC 4	MC 4	MK21	MK21	MK21	FP21	FK23	FK21									
3567	MK21	MK21	MK21	MP21	MC 4	MK23	FP21	FK23	FK21	FC 4	FK21	FK21	FC 4	FC 4	FC 4	FC 4							
3568	MC 4	MK21	MK23	MP21	MK21	MC 4	MK21	MC 4	MC 4	FP21	FK21	FK21	FK23	FK21									
3569	MS	US	FS	FP21	FK28																		
3570	MK21	MP21	MK21	MK23	MK21	FK21	FK21	FK21	FC 4	FK23	FP21												
3571	US	MP21	MK21	MK21	MC 4	MK23	MK21	FK21	FK21	FK23	FC 4	FK21	FC 4	FC 4	FP21								
3572	MP21	MK23	MK21	MC 4	MC 4	MK21	MC 4	MC 4	MK21	FP21	FC 4	FK21	FK23	FK21	FK21								
3573	MK21	MP21	FP21	MK21	MK21	MC 4	MK23	FK21	FK21	FC 4	FK23	FC 4	FK21	FC 4	FD 0	FC 4							
3574	MM 1	MK21	MK21	MC 4	MP21	MK23	MK21	MC 4	FK21	FK23	FK21	FK21	FC 4	FP21									

SEX CODE PRECEDES PUP STATUS CODE. NUMERICAL VALUE INDICATES DAY OF LACTATION.

SEX CODES: M-MALE F-FEMALE U-UNCERTAIN

PUP STATUS CODES: A-ALIVE S-STILLBORN D-DIED C-CULLED M-MISSING K-SCHEDULED SACRIFICE P-SELECTED PARENT

APPENDIX S - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP SEX AND STATUS DURING LACTATION

GROUP 4 400 MG/KG/DAY

FEMALE#	PUP #																						
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
4563	MK21	MK21	MK21	MC 4	MC 4	MP21	MK23	FP21	FK21	FC 4	FK21	FK21	FK23										
4564	MK23	MK21	MK21	MC 4	MK21	MC 4	MP21	MC 4	FP21	FK23	FK21	FK21	FC 4	FK21	FC 4								
4565	MC 4	MC 4	MK21	MK21	MM 1	MC 4	MC 4	MC 4	MK21	MC 4	MK23	MP21	FK21	FK21	FP21	FK23	FC 4	FK21					
4566	MC 4	MD12	MK21	MC 4	MP21	MK23	MK21	FK23	FC 4	FC 4	FP21	FK21	FK21	FK21									
4567	MK21	MK21	MC 4	MC 4	MC 4	MC 4	MK21	MP21	MK23	FK23	FP21	FK21	FK21	FK21	FC 4								
4568	MC 4	MC 4	MK21	MK21	MK23	MP21	MC 4	MC 4	MK21	FP21	FC 4	FK21	FK21	FK21	FK23	FC 4							
4569	MK21	MC 4	MK21	MK23	MP21	MK21	FK21	FK21	FK21	FK23	FP21	FS	FS	FS									
4570	MC 4	MP21	MK23	MK21	MK21	MK21	MC 4	FK21	FK21	FK21	FC 4	FC 4	FP21	FC 4	FC 4	FC 4	FK23	FC 4					
4571	MK21	MK21	MK23	MK21	MK21	MP21	FK23	FP21	FK21	FK21													
4572	MK21	MK21	MP21	MK21	MK23	FK21	FK21	FK21	FP21	FC 4	FC 4	FC 4	FK23										
4573	MC 4	MC 4	MC 4	MC 4	MP21	MK23	MK21	MK21	MC 4	MK21	FK21	FK21	FK23	FK21	FP21								
4574	MK21	MK21	MP21	MK21	MK23	FK23	FC 4	FK21	FK21	FK21	FC 4	FP21	FS										

SEX CODE PRECEDES PUP STATUS CODE. NUMERICAL VALUE INDICATES DAY OF LACTATION.

SEX CODES: M-MALE F-FEMALE U-UNCERTAIN

PUP STATUS CODES: A-ALIVE S-STILLBORN D-DIED C-CULLED M-MISSING K-SCHEDULED SACRIFICE P-SELECTED PARENT

APPENDIX S - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP SEX AND STATUS DURING LACTATION

GROUP 5 1000 MG/KG/DAY

FEMALE#	PUP #																						
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
5563	UZ 0	MS	FD 0	FS	FS	MM 1	MD 2	FK21	FM 1	FK23	FK21	FP21	FD 0	FP21									
5564	FS	MK23	MK21	MK21	MK21	MP21	MC 4	FC 4	FC 4	FK21	FP21	FK21	FK23	FK21									
5565	MK23	MK21	MC 4	MP21	MC 4	MK21	MC 4	MC 4	MK21	FK21	FK21	FC 4	FK23	FD 3	FK21	FC 4	FP21						
5566	MC 4	MP21	MP21	MK21	MC 4	MK21	MK23	FC 4	FC 4	FK23	FP21	FK21	FK21	FK21									
5567	MK21	MK21	MK21	MP21	MC 4	MC 4	MC 4	MK23	FK21	FC 4	FC 4	FK21	FK23	FC 4	FK21	FP21							
5568	MC 4	MK21	MK23	MK21	MP21	MC 4	MK21	FK21	FM 1	FK23	FP21	FK21	FK21	FC 4									
5569	MM 1	MK21	MK21	MC 4	MP21	MK23	MC 4	MK21	FK21	FP21	FK21	FK21	FK23										
5570	MD 0	MS	MK21	MK21	MK21	MK23	MP21	FD 1	FK23	FK21	FK21	FP21											
5571	MS	MM 1	MM 1	MD 2	MM 1	MD 1	MM 1	MD 1	FM 1	FM 1	FM 1	FM 1	FM 1	FZ 1	FD 1	FD 1							
5573	MD 1	MD 1	MD 1	FD 1	FD 1	FD 1	MD 5	MK21	MP21	MK21	MD 1	MK21	MD 1	MK28	FD 1								
5574	FD 0	MD 0	MM 1	MK23	MP21	MK21	FK23	FP21															

SEX CODE PRECEDES PUP STATUS CODE. NUMERICAL VALUE INDICATES DAY OF LACTATION.

SEX CODES: M-MALE F-FEMALE U-UNCERTAIN

PUP STATUS CODES: A-ALIVE S-STILLBORN D-DIED C-CULLED Z-CANNIBALIZED M-MISSING K-SCHEDULED SACRIFICE P-SELECTED PARENT

APPENDIX T - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 1 0 MG/KG/DAY

FEMALE#			OBSERVATIONS	DAY OF LACTATION	1 1 1 1 1 1 1 1 1 1 2 2																			
					0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9
1563	PUP#	1	WITHIN NORMAL LIMITS		P	P		P																
	PUP#	2	WITHIN NORMAL LIMITS		P	P		P		P							P						P	
	PUP#	3	WITHIN NORMAL LIMITS		P	P		P		P							P						P	
	PUP#	4	WITHIN NORMAL LIMITS		P	P		P																
	PUP#	5	WITHIN NORMAL LIMITS		P	P		P		P							P						P	
	PUP#	6	WITHIN NORMAL LIMITS		P	P		P		P							P						P	
	PUP#	7	WITHIN NORMAL LIMITS		P	P		P		P							P						P	
	PUP#	8	WITHIN NORMAL LIMITS		P	P		P		P							P						P	
	PUP#	9	WITHIN NORMAL LIMITS		P	P		P		P							P						P	
	PUP#	10	WITHIN NORMAL LIMITS		P	P		P		P							P						P	
	PUP#	11	WITHIN NORMAL LIMITS		P	P		P																
	PUP#	12	WITHIN NORMAL LIMITS		P	P		P		P							P						P	
	PUP#	13	WITHIN NORMAL LIMITS		P	P		P																
	PUP#	14	WITHIN NORMAL LIMITS		P	P		P		P							P						P	
1564	PUP#	2	WITHIN NORMAL LIMITS		P	P		P																
	PUP#	3	WITHIN NORMAL LIMITS		P	P		P																
	PUP#	4	WITHIN NORMAL LIMITS		P	P		P		P							P						P	
	PUP#	5	WITHIN NORMAL LIMITS		P	P		P		P							P						P	
	PUP#	6	WITHIN NORMAL LIMITS		P	P		P		P							P						P	
	PUP#	7	WITHIN NORMAL LIMITS		P	P		P		P							P						P	
	PUP#	8	WITHIN NORMAL LIMITS		P	P		P																
	PUP#	9	WITHIN NORMAL LIMITS		P	P		P																
	PUP#	10	WITHIN NORMAL LIMITS		P	P																		
	PUP#	11	WITHIN NORMAL LIMITS		P	P		P		P							P						P	
	PUP#	12	WITHIN NORMAL LIMITS		P	P		P		P							P						P	
	PUP#	13	WITHIN NORMAL LIMITS		P	P		P																
	PUP#	14	WITHIN NORMAL LIMITS		P	P		P															P	
	PUP#	15	WITHIN NORMAL LIMITS		P	P		P		P							P						P	
	PUP#	16	WITHIN NORMAL LIMITS		P	P		P		P							P						P	
	PUP#	17	WITHIN NORMAL LIMITS		P	P		P		P							P						P	

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX T - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 1 0 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF LACTATION	1 1 1 1 1 1 1 1 1 1 2 2																					
			0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0	1
1565	PUP# 1	WITHIN NORMAL LIMITS					P		P															
	PUP# 2	WITHIN NORMAL LIMITS					P		P		P						P							P
	PUP# 3	WITHIN NORMAL LIMITS					P		P		P						P							P
	PUP# 4	WITHIN NORMAL LIMITS					P		P															
	PUP# 5	WITHIN NORMAL LIMITS					P		P															
	PUP# 6	WITHIN NORMAL LIMITS					P		P		P						P							P
	PUP# 7	WITHIN NORMAL LIMITS					P		P		P						P							P
	PUP# 8	WITHIN NORMAL LIMITS					P		P		P						P							P
	PUP# 9	WITHIN NORMAL LIMITS					P		P		P						P							P
	PUP# 10	WITHIN NORMAL LIMITS					P		P		P						P							P
	PUP# 11	WITHIN NORMAL LIMITS					P		P															
	PUP# 12	WITHIN NORMAL LIMITS					P		P		P						P							P
	PUP# 13	WITHIN NORMAL LIMITS					P		P															
	PUP# 14	WITHIN NORMAL LIMITS					P		P															
	PUP# 15	WITHIN NORMAL LIMITS					P		P		P						P							P
	PUP# 16	WITHIN NORMAL LIMITS					P		P		P						P							P
1566	PUP# 2	WITHIN NORMAL LIMITS					P	P		P							P							P
	PUP# 3	WITHIN NORMAL LIMITS					P	P		P														
	PUP# 4	WITHIN NORMAL LIMITS					P	P		P														
	PUP# 5	WITHIN NORMAL LIMITS					P	P		P							P							P
	PUP# 6	WITHIN NORMAL LIMITS					P	P		P							P							P
	PUP# 7	WITHIN NORMAL LIMITS					P	P		P														
	PUP# 8	WITHIN NORMAL LIMITS					P	P		P														
	PUP# 9	WITHIN NORMAL LIMITS					P	P		P														
	PUP# 10	WITHIN NORMAL LIMITS					P	P		P														
	PUP# 11	WITHIN NORMAL LIMITS					P	P		P														
	PUP# 12	WITHIN NORMAL LIMITS					P	P		P							P							P
	PUP# 13	WITHIN NORMAL LIMITS					P	P		P							P							P
	PUP# 14	WITHIN NORMAL LIMITS					P	P		P							P							P
	PUP# 15	WITHIN NORMAL LIMITS					P	P		P							P							P
	PUP# 16	WITHIN NORMAL LIMITS					P	P		P							P							P
	PUP# 17	WITHIN NORMAL LIMITS					P	P		P														
	PUP# 18	WITHIN NORMAL LIMITS					P	P		P							P							P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX T - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 1 0 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF LACTATION	1 1 1 1 1 1 1 1 1 1 2 2														
			0	1	2	3	4	5	6	7	8	9	0	1	2	3	4
1566 PUP# 19	WITHIN NORMAL LIMITS		P	P		P		P					P				P
1568 PUP# 1	WITHIN NORMAL LIMITS		P	P		P											
PUP# 2	WITHIN NORMAL LIMITS		P	P		P											
PUP# 3	WITHIN NORMAL LIMITS		P	P		P		P					P				P
PUP# 4	WITHIN NORMAL LIMITS		P	P		P		P					P				P
PUP# 5	WITHIN NORMAL LIMITS		P	P		P		P					P				P
PUP# 6	WITHIN NORMAL LIMITS		P	P		P		P					P				P
PUP# 7	WITHIN NORMAL LIMITS		P	P		P		P					P				P
PUP# 8	WITHIN NORMAL LIMITS		P	P		P											
PUP# 9	WITHIN NORMAL LIMITS		P	P		P		P					P				P
PUP# 10	WITHIN NORMAL LIMITS		P	P		P		P					P				P
PUP# 11	WITHIN NORMAL LIMITS		P	P		P		P					P				P
PUP# 12	WITHIN NORMAL LIMITS		P	P		P											
PUP# 13	WITHIN NORMAL LIMITS		P	P		P		P					P				P
PUP# 14	WITHIN NORMAL LIMITS		P	P		P		P					P				P
1569 PUP# 2	WITHIN NORMAL LIMITS		P	P		P		P					P				P
PUP# 3	WITHIN NORMAL LIMITS		P	P		P		P					P				P
PUP# 4	WITHIN NORMAL LIMITS		P	P		P		P					P				P
PUP# 5	WITHIN NORMAL LIMITS		P	P		P		P					P				P
PUP# 6	WITHIN NORMAL LIMITS		P	P		P		P					P				P
PUP# 7	WITHIN NORMAL LIMITS		P	P		P		P					P				P
PUP# 8	WITHIN NORMAL LIMITS		P	P		P											
PUP# 9	WITHIN NORMAL LIMITS		P	P		P											
PUP# 10	WITHIN NORMAL LIMITS		P	P		P											
PUP# 11	WITHIN NORMAL LIMITS		P	P		P											
PUP# 12	WITHIN NORMAL LIMITS		P	P		P		P					P				P
PUP# 13	WITHIN NORMAL LIMITS		P	P		P		P					P				P
PUP# 14	WITHIN NORMAL LIMITS		P	P		P		P					P				P
PUP# 15	WITHIN NORMAL LIMITS		P	P		P											
PUP# 16	WITHIN NORMAL LIMITS		P	P		P		P					P				P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX T - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 1 0 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF LACTATION	1 1 1 1 1 1 1 1 1 1 2 2																	
			0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7
1570	PUP# 1	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 2	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 3	WITHIN NORMAL LIMITS	P	P			P			P						P				P
	PUP# 4	WITHIN NORMAL LIMITS	P	P			P			P						P				P
	PUP# 5	WITHIN NORMAL LIMITS	P	P			P			P						P				P
	PUP# 6	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 7	WITHIN NORMAL LIMITS	P	P			P			P						P				P
	PUP# 8	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 9	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 10	WITHIN NORMAL LIMITS	P	P			P			P						P				P
	PUP# 11	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 12	WITHIN NORMAL LIMITS	P	P			P			P						P				P
	PUP# 13	WITHIN NORMAL LIMITS	P	P			P			P						P				P
	PUP# 14	WITHIN NORMAL LIMITS	P	P			P			P						P				P
	PUP# 15	WITHIN NORMAL LIMITS	P	P			P			P						P				P
	PUP# 16	WITHIN NORMAL LIMITS	P	P			P			P						P				P
1571	PUP# 2	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 3	WITHIN NORMAL LIMITS	P	P			P			P						P				P
	PUP# 4	WITHIN NORMAL LIMITS	P	P			P			P						P				P
	PUP# 5	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 6	WITHIN NORMAL LIMITS	P	P			P			P						P				P
	PUP# 7	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 8	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 9	WITHIN NORMAL LIMITS	P	P			P			P						P				P
	PUP# 10	WITHIN NORMAL LIMITS	P	P			P			P						P				P
	PUP# 11	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 12	WITHIN NORMAL LIMITS	P	P			P			P						P				P
	PUP# 13	WITHIN NORMAL LIMITS	P	P			P			P						P				P
	PUP# 14	WITHIN NORMAL LIMITS	P	P			P			P						P				P
	PUP# 15	WITHIN NORMAL LIMITS	P	P			P			P						P				P
	PUP# 16	WITHIN NORMAL LIMITS	P	P			P			P						P				P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX T - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 1 0 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF LACTATION	1 1 1 1 1 1 1 1 1 1 2 2																	
			0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7
1572	PUP# 1	WITHIN NORMAL LIMITS	P	P		P		P								P				P
	PUP# 2	WITHIN NORMAL LIMITS	P	P		P		P								P				P
	PUP# 3	WITHIN NORMAL LIMITS	P	P		P		P								P				P
	PUP# 4	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 5	WITHIN NORMAL LIMITS	P	P		P		P								P				P
	PUP# 6	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 7	WITHIN NORMAL LIMITS	P	P		P		P								P				P
	PUP# 8	WITHIN NORMAL LIMITS	P	P		P		P								P				P
	PUP# 9	WITHIN NORMAL LIMITS	P	P		P		P								P				P
	PUP# 10	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 11	WITHIN NORMAL LIMITS	P	P		P		P								P				P
	PUP# 12	WITHIN NORMAL LIMITS	P	P		P		P								P				P
	PUP# 13	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 14	WITHIN NORMAL LIMITS	P	P		P		P								P				P
	PUP# 15	WITHIN NORMAL LIMITS	P	P		P														
1573	PUP# 2	WITHIN NORMAL LIMITS	P	P		P		P								P				P
	PUP# 3	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 4	WITHIN NORMAL LIMITS	P	P		P		P								P				P
	PUP# 5	WITHIN NORMAL LIMITS	P	P		P		P								P				P
	PUP# 6	WITHIN NORMAL LIMITS	P	P		P		P								P				P
	PUP# 7	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 8	WITHIN NORMAL LIMITS	P	P		P		P								P				P
	PUP# 9	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 10	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 11	WITHIN NORMAL LIMITS	P	P		P		P								P				P
	PUP# 12	WITHIN NORMAL LIMITS	P	P		P		P								P				P
	PUP# 13	WITHIN NORMAL LIMITS	P	P		P		P								P				P
	PUP# 14	WITHIN NORMAL LIMITS	P	P		P		P								P				P
	PUP# 15	WITHIN NORMAL LIMITS	P	P		P		P								P				P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX T - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 1 0 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF LACTATION	1 1 1 1 1 1 1 1 1 1 2 2																	
			0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7
1574	PUP# 1	WITHIN NORMAL LIMITS	P				P			P							P			P
	PUP# 2	WITHIN NORMAL LIMITS	P				P			P							P			P
	PUP# 3	WITHIN NORMAL LIMITS	P				P													
	PUP# 4	WITHIN NORMAL LIMITS	P				P			P							P			P
	PUP# 5	WITHIN NORMAL LIMITS	P				P			P							P			P
	PUP# 6	WITHIN NORMAL LIMITS	P				P			P										
	PUP# 7	WITHIN NORMAL LIMITS	P				P			P							P			P
	PUP# 8	WITHIN NORMAL LIMITS	P				P			P							P			P
	PUP# 9	WITHIN NORMAL LIMITS	P				P			P							P			P
	PUP# 10	WITHIN NORMAL LIMITS	P				P			P							P			P
	PUP# 11	WITHIN NORMAL LIMITS	P				P			P							P			P
	PUP# 12	WITHIN NORMAL LIMITS	P				P			P							P			P
	PUP# 13	WITHIN NORMAL LIMITS	P																	
	PUP# 14	WITHIN NORMAL LIMITS	P																	

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX T - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 2 64 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF LACTATION	1 1 1 1 1 1 1 1 1 1 2 2																	
			0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7
2563	PUP# 1	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 2	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 3	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 4	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 5	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 6	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 7	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 8	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 9	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 10	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 11	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 12	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 13	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 14	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 15	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 16	WITHIN NORMAL LIMITS	P	P		P		P									P			P
2564	PUP# 1	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 2	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 3	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 4	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 5	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 6	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 7	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 8	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 9	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 10	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 11	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 12	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 13	WITHIN NORMAL LIMITS	P	P		P		P									P			P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX T - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 2 64 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF LACTATION	1 1 1 1 1 1 1 1 1 1 2 2																					
			0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0	1
2565	PUP# 1	WITHIN NORMAL LIMITS	P	P		P			P							P								P
	PUP# 2	WITHIN NORMAL LIMITS	P	P		P			P							P								P
	PUP# 3	WITHIN NORMAL LIMITS	P	P		P			P							P								P
	PUP# 4	WITHIN NORMAL LIMITS	P	P		P																		
	PUP# 5	WITHIN NORMAL LIMITS	P	P		P			P							P								P
	PUP# 6	WITHIN NORMAL LIMITS	P	P		P																		
	PUP# 7	WITHIN NORMAL LIMITS	P	P		P																		
	PUP# 8	WITHIN NORMAL LIMITS	P	P		P																		
	PUP# 9	WITHIN NORMAL LIMITS	P	P		P																		
	PUP# 10	WITHIN NORMAL LIMITS	P	P		P			P								P							P
	PUP# 11	WITHIN NORMAL LIMITS	P	P		P			P								P							P
	PUP# 12	WITHIN NORMAL LIMITS	P	P		P			P								P							P
	PUP# 13	WITHIN NORMAL LIMITS	P	P		P			P								P							P
	PUP# 14	WITHIN NORMAL LIMITS	P	P		P			P								P							P
	PUP# 15	WITHIN NORMAL LIMITS	P	P		P			P								P							P
2566	PUP# 1	WITHIN NORMAL LIMITS	P			P			P							P								P
	PUP# 2	WITHIN NORMAL LIMITS	P			P			P							P								P
	PUP# 3	WITHIN NORMAL LIMITS	P			P			P							P								P
	PUP# 4	WITHIN NORMAL LIMITS	P			P			P							P								P
	PUP# 5	WITHIN NORMAL LIMITS	P			P																		
	PUP# 6	WITHIN NORMAL LIMITS	P			P			P							P								P
	PUP# 7	WITHIN NORMAL LIMITS	P			P			P							P								P
	PUP# 8	WITHIN NORMAL LIMITS	P			P																		
	PUP# 9	WITHIN NORMAL LIMITS	P			P																		
	PUP# 10	WITHIN NORMAL LIMITS	P			P			P							P								P
	PUP# 11	WITHIN NORMAL LIMITS	P			P			P							P								P
	PUP# 12	WITHIN NORMAL LIMITS	P			P			P							P								P
	PUP# 13	WITHIN NORMAL LIMITS	P			P			P							P								P
2567	PUP# 1	WITHIN NORMAL LIMITS	P	P		P																		
	PUP# 2	WITHIN NORMAL LIMITS	P	P		P			P							P								P
	PUP# 3	WITHIN NORMAL LIMITS	P	P		P			P							P								P
	PUP# 4	WITHIN NORMAL LIMITS	P	P		P			P							P								P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX T - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 2 64 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF LACTATION	1 1 1 1 1 1 1 1 1 1 2 2																	
			0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7
2567	PUP# 5	WITHIN NORMAL LIMITS	P	P		P				P							P			P
	PUP# 6	WITHIN NORMAL LIMITS	P	P		P				P							P			P
	PUP# 7	WITHIN NORMAL LIMITS	P	P		P				P							P			P
	PUP# 8	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 9	WITHIN NORMAL LIMITS	P	P		P				P							P			P
	PUP# 10	WITHIN NORMAL LIMITS	P	P		P				P							P			P
	PUP# 11	WITHIN NORMAL LIMITS	P	P		P				P							P			P
	PUP# 12	WITHIN NORMAL LIMITS	P	P		P				P							P			P
	PUP# 13	WITHIN NORMAL LIMITS	P	P													P			P
2568	PUP# 3	WITHIN NORMAL LIMITS	P	P		P				P							P			P
	PUP# 4	WITHIN NORMAL LIMITS	P	P		P				P							P			P
	PUP# 5	WITHIN NORMAL LIMITS	P	P		P				P							P			P
	PUP# 6	WITHIN NORMAL LIMITS	P	P		P				P							P			P
	PUP# 7	WITHIN NORMAL LIMITS	P	P		P				P							P			P
	PUP# 8	WITHIN NORMAL LIMITS	P	P		P				P							P			P
	PUP# 9	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 10	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 11	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 12	WITHIN NORMAL LIMITS	P	P		P				P							P			P
	PUP# 13	WITHIN NORMAL LIMITS	P	P		P				P							P			P
	PUP# 14	WITHIN NORMAL LIMITS	P	P		P				P							P			P
	PUP# 15	WITHIN NORMAL LIMITS	P	P		P				P							P			P
2569	PUP# 1	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 2	WITHIN NORMAL LIMITS	P	P		P				P							P			
	PUP# 3	WITHIN NORMAL LIMITS	P	P		P				P							P			P
	PUP# 4	WITHIN NORMAL LIMITS	P	P		P				P							P			P
	PUP# 5	WITHIN NORMAL LIMITS	P	P		P				P							P			
	PUP# 6	WITHIN NORMAL LIMITS	P	P		P				P							P			P
	PUP# 7	WITHIN NORMAL LIMITS	P	P		P				P							P			
	PUP# 8	WITHIN NORMAL LIMITS	P	P		P				P							P			
	PUP# 9	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 10	WITHIN NORMAL LIMITS	P	P		P														

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX T - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 2 64 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF LACTATION	1 1 1 1 1 1 1 1 1 1 2 2																	
			0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7
2569	PUP# 11	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 12	WITHIN NORMAL LIMITS	P	P		P		P							P					
	PUP# 13	WITHIN NORMAL LIMITS	P	P		P		P							P					
	PUP# 14	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 15	WITHIN NORMAL LIMITS	P	P		P		P							P					
	PUP# 2	ALOPECIA - EXTREMITIES/SNOUT																		2
	PUP# 5	ALOPECIA - EXTREMITIES/SNOUT																		2
	PUP# 7	ALOPECIA - EXTREMITIES/SNOUT																		2
	PUP# 8	ALOPECIA - EXTREMITIES/SNOUT																		2
	PUP# 12	ALOPECIA - EXTREMITIES/SNOUT																		2
	PUP# 13	ALOPECIA - EXTREMITIES/SNOUT																		2
	PUP# 15	ALOPECIA - EXTREMITIES/SNOUT																		2
2570	PUP# 1	WITHIN NORMAL LIMITS	P			P		P							P					P
	PUP# 2	WITHIN NORMAL LIMITS	P			P		P							P					P
	PUP# 3	WITHIN NORMAL LIMITS	P			P		P							P					P
	PUP# 4	WITHIN NORMAL LIMITS	P			P		P							P					P
	PUP# 5	WITHIN NORMAL LIMITS	P			P		P							P					P
	PUP# 6	WITHIN NORMAL LIMITS	P			P														
	PUP# 7	WITHIN NORMAL LIMITS	P			P														
	PUP# 8	WITHIN NORMAL LIMITS	P			P		P							P					P
	PUP# 9	WITHIN NORMAL LIMITS	P			P		P							P					P
	PUP# 10	WITHIN NORMAL LIMITS	P			P		P							P					P
	PUP# 11	WITHIN NORMAL LIMITS	P			P		P							P					P
	PUP# 12	WITHIN NORMAL LIMITS	P			P														
	PUP# 13	WITHIN NORMAL LIMITS	P			P														
	PUP# 14	WITHIN NORMAL LIMITS	P			P		P							P					P
2571	PUP# 1	WITHIN NORMAL LIMITS	P	P		P		P							P					P
	PUP# 2	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 3	WITHIN NORMAL LIMITS	P	P		P		P							P					P
	PUP# 4	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 5	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 6	WITHIN NORMAL LIMITS	P	P		P														

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX T - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 2 64 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF LACTATION	1 1 1 1 1 1 1 1 1 1 2 2																	
			0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7
2571	PUP# 7	WITHIN NORMAL LIMITS	P	P			P			P							P			P
	PUP# 8	WITHIN NORMAL LIMITS	P	P			P			P							P			P
	PUP# 9	WITHIN NORMAL LIMITS	P	P			P			P							P			P
	PUP# 10	WITHIN NORMAL LIMITS	P	P			P			P							P			P
	PUP# 11	WITHIN NORMAL LIMITS	P	P			P			P							P			P
	PUP# 12	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 13	WITHIN NORMAL LIMITS	P	P			P			P							P			P
	PUP# 14	WITHIN NORMAL LIMITS	P	P			P			P							P			P
	PUP# 15	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 16	WITHIN NORMAL LIMITS	P	P			P			P							P			P
2573	PUP# 1	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 2	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 3	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 4	WITHIN NORMAL LIMITS	P	P			P			P							P			P
	PUP# 5	WITHIN NORMAL LIMITS	P	P			P			P							P			P
	PUP# 6	WITHIN NORMAL LIMITS	P	P			P			P							P			P
	PUP# 7	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 8	WITHIN NORMAL LIMITS	P	P			P			P							P			P
	PUP# 9	WITHIN NORMAL LIMITS	P	P			P			P										
	PUP# 10	WITHIN NORMAL LIMITS	P	P			P			P							P			P
	PUP# 11	WITHIN NORMAL LIMITS	P	P			P			P							P			P
	PUP# 12	WITHIN NORMAL LIMITS	P	P			P			P							P			P
	PUP# 13	WITHIN NORMAL LIMITS	P	P			P			P							P			P
	PUP# 14	WITHIN NORMAL LIMITS	P	P			P			P							P			P
	PUP# 15	WITHIN NORMAL LIMITS	P	P			P			P							P			P
2574	PUP# 1	WITHIN NORMAL LIMITS	P	P			P			P							P			P
	PUP# 2	WITHIN NORMAL LIMITS	P	P			P			P							P			P
	PUP# 3	WITHIN NORMAL LIMITS	P	P			P			P							P			P
	PUP# 4	WITHIN NORMAL LIMITS	P	P			P			P							P			P
	PUP# 5	WITHIN NORMAL LIMITS	P	P			P			P							P			P
	PUP# 6	WITHIN NORMAL LIMITS	P	P			P			P							P			P
	PUP# 7	WITHIN NORMAL LIMITS	P	P			P			P							P			P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

6-FEB-2004 10:08

Huntingdon Life Sciences 03-4254

PAGE 260

APPENDIX T - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 2 64 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF LACTATION	1 1 1 1 1 1 1 1 1 1 2 2																	
			0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7
2574 PUP# 8	WITHIN NORMAL LIMITS		P	P		P			P							P				P
PUP# 9	WITHIN NORMAL LIMITS		P	P		P			P							P				P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX T - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 3 160 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF LACTATION	1 1 1 1 1 1 1 1 1 1 2 2																	
			0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7
3563	PUP# 1	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 2	WITHIN NORMAL LIMITS	P	P			P		P					P						P
	PUP# 3	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 4	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 5	WITHIN NORMAL LIMITS	P	P			P		P					P						P
	PUP# 6	WITHIN NORMAL LIMITS	P	P			P		P					P						P
	PUP# 7	WITHIN NORMAL LIMITS	P	P			P		P					P						P
	PUP# 8	WITHIN NORMAL LIMITS	P																	
	PUP# 9	WITHIN NORMAL LIMITS	P	P			P		P					P						P
	PUP# 10	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 11	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 12	WITHIN NORMAL LIMITS	P	P			P		P					P						P
	PUP# 13	WITHIN NORMAL LIMITS	P	P			P		P					P						P
	PUP# 14	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 15	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 16	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 17	WITHIN NORMAL LIMITS	P	P			P		P					P						P
	PUP# 18	WITHIN NORMAL LIMITS	P	P			P		P					P						P
	PUP# 19	WITHIN NORMAL LIMITS	P	P			P		P					P						P
3564	PUP# 1	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 2	WITHIN NORMAL LIMITS	P	P			P		P					P						P
	PUP# 3	WITHIN NORMAL LIMITS	P	P			P		P					P						P
	PUP# 4	WITHIN NORMAL LIMITS	P	P			P		P					P						P
	PUP# 5	WITHIN NORMAL LIMITS	P	P			P		P					P						P
	PUP# 6	WITHIN NORMAL LIMITS	P	P			P		P					P						P
	PUP# 7	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 8	WITHIN NORMAL LIMITS	P	P			P		P					P						P
	PUP# 9	WITHIN NORMAL LIMITS	P	P			P		P					P						P
	PUP# 10	WITHIN NORMAL LIMITS	P	P			P		P					P						P
	PUP# 11	WITHIN NORMAL LIMITS	P	P			P		P					P						P
	PUP# 12	WITHIN NORMAL LIMITS	P	P			P		P					P						P
	PUP# 13	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 14	WITHIN NORMAL LIMITS	P	P			P													

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX T - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 3 160 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF LACTATION	1 1 1 1 1 1 1 1 1 1 2 2																	
			0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7
3564	PUP# 15	WITHIN NORMAL LIMITS	P	P		P														
3565	PUP# 1	WITHIN NORMAL LIMITS	P	P		P		P					P							P
	PUP# 2	WITHIN NORMAL LIMITS	P	P		P		P					P							P
	PUP# 3	WITHIN NORMAL LIMITS	P	P		P		P					P							P
	PUP# 4	WITHIN NORMAL LIMITS	P	P		P		P					P							P
	PUP# 5	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 6	WITHIN NORMAL LIMITS	P	P		P		P					P							P
	PUP# 7	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 8	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 9	WITHIN NORMAL LIMITS	P	P		P		P					P							P
	PUP# 10	WITHIN NORMAL LIMITS	P	P		P		P					P							P
	PUP# 11	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 12	WITHIN NORMAL LIMITS	P	P		P		P					P							P
	PUP# 13	WITHIN NORMAL LIMITS	P	P		P		P					P							P
	PUP# 14	WITHIN NORMAL LIMITS	P	P		P		P					P							P
	PUP# 15	WITHIN NORMAL LIMITS	P	P		P														
3566	PUP# 1	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 2	WITHIN NORMAL LIMITS	P	P		P		P					P							P
	PUP# 3	WITHIN NORMAL LIMITS	P	P		P		P					P							P
	PUP# 4	WITHIN NORMAL LIMITS	P	P		P		P					P							P
	PUP# 5	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 6	WITHIN NORMAL LIMITS	P	P		P		P					P							P
	PUP# 7	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 8	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 9	WITHIN NORMAL LIMITS	P	P		P		P					P							P
	PUP# 10	WITHIN NORMAL LIMITS	P	P		P		P					P							P
	PUP# 11	WITHIN NORMAL LIMITS	P	P		P		P					P							P
	PUP# 12	WITHIN NORMAL LIMITS	P	P		P		P					P							P
	PUP# 13	WITHIN NORMAL LIMITS	P	P		P		P					P							P
	PUP# 14	WITHIN NORMAL LIMITS	P	P		P		P					P							P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX T - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 3 160 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF LACTATION	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1																	
			0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7
3567	PUP# 1	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 2	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 3	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 4	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 5	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 6	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 7	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 8	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 9	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 10	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 11	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 12	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 13	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 14	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 15	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 16	WITHIN NORMAL LIMITS	P	P			P													
3568	PUP# 1	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 2	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 3	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 4	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 5	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 6	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 7	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 8	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 9	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 10	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 11	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 12	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 13	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 14	WITHIN NORMAL LIMITS	P	P			P		P								P			P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX T - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 3 160 MG/KG/DAY

FEMALE#			OBSERVATIONS	DAY OF LACTATION	1 1 1 1 1 1 1 1 1 1 1 1 2 2																			
					0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9
3569	PUP#	4	WITHIN NORMAL LIMITS		P	P		P		P						P								P
	PUP#	5	WITHIN NORMAL LIMITS		P	P		P		P						P								P
3570	PUP#	1	WITHIN NORMAL LIMITS		P	P		P		P						P								P
	PUP#	2	WITHIN NORMAL LIMITS		P	P		P		P						P								P
	PUP#	3	WITHIN NORMAL LIMITS		P	P		P		P						P								P
	PUP#	4	WITHIN NORMAL LIMITS		P	P		P		P						P								P
	PUP#	5	WITHIN NORMAL LIMITS		P	P		P		P						P								P
	PUP#	6	WITHIN NORMAL LIMITS		P	P		P		P						P								P
	PUP#	7	WITHIN NORMAL LIMITS		P	P		P		P						P								P
	PUP#	8	WITHIN NORMAL LIMITS		P	P		P		P						P								P
	PUP#	9	WITHIN NORMAL LIMITS		P	P		P								P								P
	PUP#	10	WITHIN NORMAL LIMITS		P	P		P		P						P								P
	PUP#	11	WITHIN NORMAL LIMITS		P	P		P		P						P								P
3571	PUP#	2	WITHIN NORMAL LIMITS		P	P		P		P						P								P
	PUP#	3	WITHIN NORMAL LIMITS		P	P		P		P						P								P
	PUP#	4	WITHIN NORMAL LIMITS		P	P		P		P						P								P
	PUP#	5	WITHIN NORMAL LIMITS		P	P		P																
	PUP#	6	WITHIN NORMAL LIMITS		P	P		P		P						P								P
	PUP#	7	WITHIN NORMAL LIMITS		P	P		P		P						P								P
	PUP#	8	WITHIN NORMAL LIMITS		P	P		P		P						P								P
	PUP#	9	WITHIN NORMAL LIMITS		P	P		P		P						P								P
	PUP#	10	WITHIN NORMAL LIMITS		P	P		P		P						P								P
	PUP#	11	WITHIN NORMAL LIMITS		P	P		P																
	PUP#	12	WITHIN NORMAL LIMITS		P	P		P		P						P								P
	PUP#	13	WITHIN NORMAL LIMITS		P	P		P																
	PUP#	14	WITHIN NORMAL LIMITS		P	P		P																
	PUP#	15	WITHIN NORMAL LIMITS		P	P		P		P						P								P
	3572	PUP#	1	WITHIN NORMAL LIMITS		P	P		P		P						P							
PUP#		2	WITHIN NORMAL LIMITS		P	P		P		P						P								P
PUP#		3	WITHIN NORMAL LIMITS		P	P		P		P						P								P
PUP#		4	WITHIN NORMAL LIMITS		P	P		P																

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX T - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 3 160 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF LACTATION	1 1 1 1 1 1 1 1 1 1 2 2																	
			0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7
3572	PUP# 5	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 6	WITHIN NORMAL LIMITS	P	P			P		P					P						P
	PUP# 7	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 8	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 9	WITHIN NORMAL LIMITS	P	P			P		P					P						P
	PUP# 10	WITHIN NORMAL LIMITS	P	P			P		P					P						P
	PUP# 11	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 12	WITHIN NORMAL LIMITS	P	P			P		P					P						P
	PUP# 13	WITHIN NORMAL LIMITS	P	P			P		P					P						P
	PUP# 14	WITHIN NORMAL LIMITS	P	P			P		P					P						P
	PUP# 15	WITHIN NORMAL LIMITS	P	P			P		P					P						P
3573	PUP# 1	WITHIN NORMAL LIMITS	P	P			P		P					P						P
	PUP# 2	WITHIN NORMAL LIMITS	P	P			P		P					P						P
	PUP# 3	WITHIN NORMAL LIMITS	P	P			P		P					P						P
	PUP# 4	WITHIN NORMAL LIMITS	P	P			P		P					P						P
	PUP# 5	WITHIN NORMAL LIMITS	P	P			P		P					P						P
	PUP# 6	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 7	WITHIN NORMAL LIMITS	P	P			P		P					P						P
	PUP# 8	WITHIN NORMAL LIMITS	P	P			P		P					P						P
	PUP# 9	WITHIN NORMAL LIMITS	P	P			P		P					P						P
	PUP# 10	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 11	WITHIN NORMAL LIMITS	P	P			P		P					P						P
	PUP# 12	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 13	WITHIN NORMAL LIMITS	P	P			P		P					P						P
	PUP# 14	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 15	WITHIN NORMAL LIMITS	P																	
	PUP# 16	WITHIN NORMAL LIMITS	P	P			P													
3574	PUP# 1	WITHIN NORMAL LIMITS	P																	
	PUP# 2	WITHIN NORMAL LIMITS	P	P			P		P					P						P
	PUP# 3	WITHIN NORMAL LIMITS	P	P			P		P					P						P
	PUP# 4	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 5	WITHIN NORMAL LIMITS	P	P			P		P					P						P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

6-FEB-2004 10:08

Huntingdon Life Sciences 03-4254

PAGE 266

APPENDIX T - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 3 160 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF LACTATION	1 1 1 1 1 1 1 1 1 1 1 1 1 1 2 2																							
			0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0	1		
3574	PUP# 6	WITHIN NORMAL LIMITS	P	P		P			P							P								P		
	PUP# 7	WITHIN NORMAL LIMITS	P	P		P			P							P							P			
	PUP# 8	WITHIN NORMAL LIMITS	P	P		P																				
	PUP# 9	WITHIN NORMAL LIMITS	P	P		P			P							P							P			
	PUP# 10	WITHIN NORMAL LIMITS	P	P		P			P							P							P			
	PUP# 11	WITHIN NORMAL LIMITS	P	P		P			P							P							P			
	PUP# 12	WITHIN NORMAL LIMITS	P	P		P			P							P							P			
	PUP# 13	WITHIN NORMAL LIMITS	P	P		P																				
	PUP# 14	WITHIN NORMAL LIMITS	P			P			P							P							P			
	PUP# 14	PALE		P																						

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX T - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 4 400 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF LACTATION	1 1 1 1 1 1 1 1 1 1 2 2																	
			0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7
4563	PUP# 1	WITHIN NORMAL LIMITS	P	P		P		P					P							P
	PUP# 2	WITHIN NORMAL LIMITS	P	P		P		P					P							P
	PUP# 3	WITHIN NORMAL LIMITS	P	P		P		P					P							P
	PUP# 4	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 5	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 6	WITHIN NORMAL LIMITS	P	P		P		P					P							P
	PUP# 7	WITHIN NORMAL LIMITS	P	P		P		P					P							P
	PUP# 8	WITHIN NORMAL LIMITS	P	P		P		P					P							P
	PUP# 9	WITHIN NORMAL LIMITS	P	P		P		P					P							P
	PUP# 10	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 11	WITHIN NORMAL LIMITS	P	P		P		P					P							P
	PUP# 12	WITHIN NORMAL LIMITS	P	P		P		P					P							P
	PUP# 13	WITHIN NORMAL LIMITS	P	P		P		P					P							P
4564	PUP# 1	WITHIN NORMAL LIMITS	P	P		P		P					P							P
	PUP# 2	WITHIN NORMAL LIMITS	P	P		P		P					P							P
	PUP# 3	WITHIN NORMAL LIMITS	P	P		P		P					P							P
	PUP# 4	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 5	WITHIN NORMAL LIMITS	P	P		P		P					P							P
	PUP# 6	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 7	WITHIN NORMAL LIMITS	P	P		P		P					P							P
	PUP# 8	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 9	WITHIN NORMAL LIMITS	P	P		P		P					P							P
	PUP# 10	WITHIN NORMAL LIMITS	P	P		P		P					P							P
	PUP# 11	WITHIN NORMAL LIMITS	P	P		P		P					P							P
	PUP# 12	WITHIN NORMAL LIMITS	P	P		P		P					P							P
	PUP# 13	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 14	WITHIN NORMAL LIMITS	P	P		P		P					P							P
	PUP# 15	WITHIN NORMAL LIMITS	P	P		P														
4565	PUP# 1	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 2	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 3	WITHIN NORMAL LIMITS	P	P		P		P					P							P
	PUP# 4	WITHIN NORMAL LIMITS	P	P		P		P					P							P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX T - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 4 400 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF LACTATION	1 1 1 1 1 1 1 1 1 1 2 2																	
			0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7
4565	PUP# 5	WITHIN NORMAL LIMITS	P																	
	PUP# 6	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 7	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 8	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 9	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 10	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 11	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 12	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 13	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 14	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 15	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 16	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 17	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 18	WITHIN NORMAL LIMITS	P	P		P		P									P			P
4566	PUP# 1	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 2	WITHIN NORMAL LIMITS	P	P		P		P												
	PUP# 3	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 4	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 5	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 6	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 7	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 8	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 9	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 10	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 11	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 12	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 13	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 14	WITHIN NORMAL LIMITS	P	P		P		P									P			P
4567	PUP# 1	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 2	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 3	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 4	WITHIN NORMAL LIMITS	P	P		P														

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX T - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 4 400 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF LACTATION	1 1 1 1 1 1 1 1 1 1 2 2																	
			0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7
4567	PUP# 5	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 6	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 7	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 8	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 9	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 10	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 11	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 12	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 13	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 14	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 15	WITHIN NORMAL LIMITS	P	P			P													
4568	PUP# 1	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 2	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 3	WITHIN NORMAL LIMITS	P	P			P		P											P
	PUP# 4	WITHIN NORMAL LIMITS	P	P			P		P											P
	PUP# 5	WITHIN NORMAL LIMITS	P	P			P		P											P
	PUP# 6	WITHIN NORMAL LIMITS	P	P			P		P											P
	PUP# 7	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 8	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 9	WITHIN NORMAL LIMITS	P	P			P		P											P
	PUP# 10	WITHIN NORMAL LIMITS	P	P			P		P											P
	PUP# 11	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 12	WITHIN NORMAL LIMITS	P	P			P		P											P
	PUP# 13	WITHIN NORMAL LIMITS	P	P			P		P											P
	PUP# 14	WITHIN NORMAL LIMITS	P	P			P		P											P
	PUP# 15	WITHIN NORMAL LIMITS	P	P			P		P											P
	PUP# 16	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 3	ALOPECIA - GENERAL																2		
	PUP# 4	ALOPECIA - GENERAL																2		
	PUP# 5	ALOPECIA - GENERAL																2		
	PUP# 6	ALOPECIA - GENERAL																2		
	PUP# 9	ALOPECIA - GENERAL																2		
	PUP# 10	ALOPECIA - GENERAL																2		

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX T - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 4 400 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF LACTATION	1 1 1 1 1 1 1 1 1 1 2 2																	
			0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7
4568	PUP# 12 ALOPECIA - GENERAL																			2
	PUP# 13 ALOPECIA - GENERAL																			2
	PUP# 14 ALOPECIA - GENERAL																			2
	PUP# 15 ALOPECIA - GENERAL																			2
4569	PUP# 1 WITHIN NORMAL LIMITS		P				P			P								P		P
	PUP# 2 WITHIN NORMAL LIMITS		P				P													
	PUP# 3 WITHIN NORMAL LIMITS		P				P			P								P		P
	PUP# 4 WITHIN NORMAL LIMITS		P				P			P								P		P
	PUP# 5 WITHIN NORMAL LIMITS		P				P			P								P		P
	PUP# 6 WITHIN NORMAL LIMITS		P				P			P								P		P
	PUP# 7 WITHIN NORMAL LIMITS		P				P			P								P		P
	PUP# 8 WITHIN NORMAL LIMITS		P				P			P								P		P
	PUP# 9 WITHIN NORMAL LIMITS		P				P			P								P		P
	PUP# 10 WITHIN NORMAL LIMITS		P				P			P								P		P
	PUP# 11 WITHIN NORMAL LIMITS		P				P			P								P		P
4570	PUP# 1 WITHIN NORMAL LIMITS		P	P			P													
	PUP# 2 WITHIN NORMAL LIMITS		P	P			P			P								P		P
	PUP# 3 WITHIN NORMAL LIMITS		P	P			P			P								P		P
	PUP# 4 WITHIN NORMAL LIMITS		P	P			P			P								P		P
	PUP# 5 WITHIN NORMAL LIMITS		P	P			P			P								P		P
	PUP# 6 WITHIN NORMAL LIMITS		P	P			P			P								P		P
	PUP# 7 WITHIN NORMAL LIMITS		P	P			P													
	PUP# 8 WITHIN NORMAL LIMITS		P	P			P			P								P		P
	PUP# 9 WITHIN NORMAL LIMITS		P	P			P			P								P		P
	PUP# 10 WITHIN NORMAL LIMITS		P	P			P			P								P		P
	PUP# 11 WITHIN NORMAL LIMITS		P	P			P													
	PUP# 12 WITHIN NORMAL LIMITS		P	P			P													
	PUP# 13 WITHIN NORMAL LIMITS		P	P			P			P								P		P
	PUP# 14 WITHIN NORMAL LIMITS		P	P			P													
	PUP# 15 WITHIN NORMAL LIMITS		P	P			P													
	PUP# 16 WITHIN NORMAL LIMITS		P	P			P													
	PUP# 17 WITHIN NORMAL LIMITS		P	P			P			P								P		P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX T - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 4 400 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF LACTATION	1 1 1 1 1 1 1 1 1 1 2 2																	
			0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7
4570	PUP# 18	WITHIN NORMAL LIMITS	P	P			P													
4571	PUP# 1	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 2	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 3	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 4	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 5	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 6	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 7	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 8	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 9	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 10	WITHIN NORMAL LIMITS	P	P			P		P								P			P
4572	PUP# 1	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 2	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 3	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 4	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 5	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 6	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 7	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 8	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 9	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 10	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 11	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 12	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 13	WITHIN NORMAL LIMITS	P	P			P		P								P			P
4573	PUP# 1	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 2	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 3	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 4	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 5	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 6	WITHIN NORMAL LIMITS	P	P			P		P								P			P
	PUP# 7	WITHIN NORMAL LIMITS	P	P			P		P								P			P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX T - F1 GENERATION

TEA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 4 400 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF LACTATION	1 1 1 1 1 1 1 1 1 1 2 2																	
			0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7
4573	PUP# 8	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 9	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 10	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 11	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 12	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 13	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 14	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 15	WITHIN NORMAL LIMITS	P	P		P		P									P			P
4574	PUP# 1	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 2	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 3	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 4	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 5	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 6	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 7	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 8	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 9	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 10	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 11	WITHIN NORMAL LIMITS	P	P		P														
	PUP# 12	WITHIN NORMAL LIMITS	P	P		P		P									P			P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX T - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 5 1000 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF LACTATION	1 1 1 1 1 1 1 1 1 1 2 2																	
			0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7
5563	PUP# 6	WITHIN NORMAL LIMITS	P																	
	PUP# 7	WITHIN NORMAL LIMITS	P	P																
	PUP# 8	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 9	WITHIN NORMAL LIMITS	P																	
	PUP# 10	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 11	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 12	WITHIN NORMAL LIMITS	P	P		P		P									P			P
	PUP# 13	WITHIN NORMAL LIMITS	P																	
	PUP# 14	WITHIN NORMAL LIMITS	P	P		P		P									P			P
5564	PUP# 2	WITHIN NORMAL LIMITS	P				P		P								P			P
	PUP# 3	WITHIN NORMAL LIMITS	P				P		P								P			P
	PUP# 4	WITHIN NORMAL LIMITS	P				P		P								P			P
	PUP# 5	WITHIN NORMAL LIMITS	P				P		P								P			P
	PUP# 6	WITHIN NORMAL LIMITS	P				P		P								P			P
	PUP# 7	WITHIN NORMAL LIMITS	P				P		P											
	PUP# 8	WITHIN NORMAL LIMITS	P				P													
	PUP# 9	WITHIN NORMAL LIMITS	P				P		P											
	PUP# 10	WITHIN NORMAL LIMITS	P				P		P								P			P
	PUP# 11	WITHIN NORMAL LIMITS	P				P		P								P			P
	PUP# 12	WITHIN NORMAL LIMITS	P				P		P								P			P
	PUP# 13	WITHIN NORMAL LIMITS	P				P		P								P			P
	PUP# 14	WITHIN NORMAL LIMITS	P				P		P								P			P
5565	PUP# 1	WITHIN NORMAL LIMITS	P				P		P								P			P
	PUP# 2	WITHIN NORMAL LIMITS	P				P		P								P			P
	PUP# 3	WITHIN NORMAL LIMITS	P				P													
	PUP# 4	WITHIN NORMAL LIMITS	P				P		P								P			P
	PUP# 5	WITHIN NORMAL LIMITS	P				P		P											
	PUP# 6	WITHIN NORMAL LIMITS	P				P		P								P			P
	PUP# 7	WITHIN NORMAL LIMITS	P				P		P											
	PUP# 8	WITHIN NORMAL LIMITS	P				P		P											
	PUP# 9	WITHIN NORMAL LIMITS	P				P		P								P			P
	PUP# 10	WITHIN NORMAL LIMITS	P				P		P								P			P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX T - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 5 1000 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF LACTATION	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1																	
			0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7
5565	PUP# 11	WITHIN NORMAL LIMITS	P				P			P							P			P
	PUP# 12	WITHIN NORMAL LIMITS	P				P													
	PUP# 13	WITHIN NORMAL LIMITS	P				P			P							P			P
	PUP# 14	WITHIN NORMAL LIMITS	P																	
	PUP# 15	WITHIN NORMAL LIMITS	P				P			P							P			P
	PUP# 16	WITHIN NORMAL LIMITS	P				P													
	PUP# 17	WITHIN NORMAL LIMITS	P				P			P							P			P
5566	PUP# 1	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 2	WITHIN NORMAL LIMITS	P	P			P			P							P			P
	PUP# 3	WITHIN NORMAL LIMITS	P	P			P			P							P			P
	PUP# 4	WITHIN NORMAL LIMITS	P	P			P										P			P
	PUP# 5	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 6	WITHIN NORMAL LIMITS	P	P			P			P							P			P
	PUP# 7	WITHIN NORMAL LIMITS	P	P			P			P							P			P
	PUP# 8	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 9	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 10	WITHIN NORMAL LIMITS	P	P			P			P							P			P
	PUP# 11	WITHIN NORMAL LIMITS	P	P			P			P							P			P
	PUP# 12	WITHIN NORMAL LIMITS	P	P			P			P							P			P
	PUP# 13	WITHIN NORMAL LIMITS	P	P			P			P							P			P
	PUP# 14	WITHIN NORMAL LIMITS	P	P			P			P							P			P
	PUP# 4	TOE APPEARS DAMAGED								P										
5567	PUP# 1	WITHIN NORMAL LIMITS	P	P			P			P							P			P
	PUP# 2	WITHIN NORMAL LIMITS	P	P			P			P							P			P
	PUP# 3	WITHIN NORMAL LIMITS	P	P			P			P							P			P
	PUP# 4	WITHIN NORMAL LIMITS	P	P			P			P							P			P
	PUP# 5	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 6	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 7	WITHIN NORMAL LIMITS	P	P			P													
	PUP# 8	WITHIN NORMAL LIMITS	P	P			P			P							P			P
	PUP# 9	WITHIN NORMAL LIMITS	P	P			P			P							P			P
	PUP# 10	WITHIN NORMAL LIMITS	P	P			P													

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX T - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 5 1000 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF LACTATION	1 1 1 1 1 1 1 1 1 1 2 2																							
			0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0	1		
5567	PUP# 11	WITHIN NORMAL LIMITS	P	P		P																				
	PUP# 12	WITHIN NORMAL LIMITS	P	P		P		P								P							P			
	PUP# 13	WITHIN NORMAL LIMITS	P	P		P		P								P							P			
	PUP# 14	WITHIN NORMAL LIMITS	P	P		P																				
	PUP# 15	WITHIN NORMAL LIMITS	P	P		P		P								P							P			
	PUP# 16	WITHIN NORMAL LIMITS	P	P		P		P								P							P			
5568	PUP# 1	WITHIN NORMAL LIMITS	P	P		P																				
	PUP# 2	WITHIN NORMAL LIMITS	P	P		P		P								P							P			
	PUP# 3	WITHIN NORMAL LIMITS	P	P		P		P								P							P			
	PUP# 4	WITHIN NORMAL LIMITS	P	P		P		P								P							P			
	PUP# 5	WITHIN NORMAL LIMITS	P	P		P		P								P							P			
	PUP# 6	WITHIN NORMAL LIMITS	P	P		P																				
	PUP# 7	WITHIN NORMAL LIMITS	P	P		P		P								P							P			
	PUP# 8	WITHIN NORMAL LIMITS	P	P		P		P								P							P			
	PUP# 9	WITHIN NORMAL LIMITS	P																							
	PUP# 10	WITHIN NORMAL LIMITS	P	P		P		P								P							P			
	PUP# 11	WITHIN NORMAL LIMITS	P	P		P		P								P							P			
	PUP# 12	WITHIN NORMAL LIMITS	P	P		P		P								P							P			
	PUP# 13	WITHIN NORMAL LIMITS	P	P		P		P								P							P			
	PUP# 14	WITHIN NORMAL LIMITS	P	P		P																				
5569	PUP# 1	WITHIN NORMAL LIMITS	P																							
	PUP# 2	WITHIN NORMAL LIMITS	P	P		P		P								P							P			
	PUP# 3	WITHIN NORMAL LIMITS	P	P		P		P								P							P			
	PUP# 4	WITHIN NORMAL LIMITS	P	P		P																				
	PUP# 5	WITHIN NORMAL LIMITS	P	P		P		P								P							P			
	PUP# 6	WITHIN NORMAL LIMITS	P	P		P		P								P							P			
	PUP# 7	WITHIN NORMAL LIMITS	P	P		P																				
	PUP# 8	WITHIN NORMAL LIMITS	P	P		P		P								P							P			
	PUP# 9	WITHIN NORMAL LIMITS	P	P		P		P								P							P			
	PUP# 10	WITHIN NORMAL LIMITS	P	P		P		P								P							P			
	PUP# 11	WITHIN NORMAL LIMITS	P	P		P		P								P							P			
	PUP# 12	WITHIN NORMAL LIMITS	P	P		P		P								P							P			

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX T - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 5 1000 MG/KG/DAY

FEMALE#			OBSERVATIONS	DAY OF LACTATION	1 1 1 1 1 1 1 1 1 1 2 2																			
					0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9
5569	PUP#	13	WITHIN NORMAL LIMITS		P	P			P							P								P
5570	PUP#	3	WITHIN NORMAL LIMITS		P				P							P								P
	PUP#	4	WITHIN NORMAL LIMITS		P				P							P								P
	PUP#	5	WITHIN NORMAL LIMITS		P				P							P								P
	PUP#	6	WITHIN NORMAL LIMITS		P				P							P								P
	PUP#	7	WITHIN NORMAL LIMITS		P				P							P								
	PUP#	8	WITHIN NORMAL LIMITS		P																			
	PUP#	9	WITHIN NORMAL LIMITS		P				P							P								P
	PUP#	10	WITHIN NORMAL LIMITS		P				P							P								P
	PUP#	11	WITHIN NORMAL LIMITS		P				P							P								P
	PUP#	12	WITHIN NORMAL LIMITS		P				P							P								P
	PUP#	7	DIGIT MISSING																				P	
5571	PUP#	2	WITHIN NORMAL LIMITS		P																			
	PUP#	3	WITHIN NORMAL LIMITS		P																			
	PUP#	4	WITHIN NORMAL LIMITS		P	P																		
	PUP#	5	WITHIN NORMAL LIMITS		P																			
	PUP#	6	WITHIN NORMAL LIMITS		P																			
	PUP#	7	WITHIN NORMAL LIMITS		P																			
	PUP#	8	WITHIN NORMAL LIMITS		P																			
	PUP#	9	WITHIN NORMAL LIMITS		P																			
	PUP#	10	WITHIN NORMAL LIMITS		P																			
	PUP#	11	WITHIN NORMAL LIMITS		P																			
	PUP#	12	WITHIN NORMAL LIMITS		P																			
	PUP#	13	WITHIN NORMAL LIMITS		P																			
	PUP#	14	WITHIN NORMAL LIMITS		P																			
	PUP#	15	WITHIN NORMAL LIMITS		P																			
	PUP#	16	WITHIN NORMAL LIMITS		P																			
5573	PUP#	8	WITHIN NORMAL LIMITS		P	P			P							P								P
	PUP#	9	WITHIN NORMAL LIMITS		P	P			P							P								P
	PUP#	10	WITHIN NORMAL LIMITS		P	P			P							P								P
	PUP#	11	WITHIN NORMAL LIMITS		P	P																		

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX T - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 5 1000 MG/KG/DAY

FEMALE#	OBSERVATIONS	DAY OF LACTATION	1 1 1 1 1 1 1 1 1 1 2 2																		
			0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8
5573	PUP# 12	WITHIN NORMAL LIMITS	P	P		P			P								P				P
	PUP# 13	WITHIN NORMAL LIMITS	P																		
	PUP# 14	WITHIN NORMAL LIMITS	P	P		P			P								P				P
	PUP# 15	WITHIN NORMAL LIMITS	P	P																	
	PUP# 7	SCABS					P														
	PUP# 7	ULCERATION	P	P																	
5574	PUP# 2	WITHIN NORMAL LIMITS	P																		
	PUP# 3	WITHIN NORMAL LIMITS	P																		
	PUP# 4	WITHIN NORMAL LIMITS	P	P		P			P								P				P
	PUP# 5	WITHIN NORMAL LIMITS	P	P		P			P								P				P
	PUP# 6	WITHIN NORMAL LIMITS	P	P		P			P								P				P
	PUP# 7	WITHIN NORMAL LIMITS	P	P		P			P								P				P
	PUP# 8	WITHIN NORMAL LIMITS	P	P		P			P								P				P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

6-FEB-2004 10:09

Huntingdon Life Sciences 03-4254

PAGE 278

APPENDIX U - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

GROUP 1		INDIVIDUAL PUP BODY WEIGHTS (GRAMS)														LACTATION DAY 1					
FEMALE#	MEAN	0 MG/KG/DAY																			
		PUP#	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
1563	7.3	7.5	7.7	8.1	8.1	6.8	7.8	6.7	7.2	6.7	7.6	7.3	7.3	6.9	7.2						
1564	6.8	S	7.3	6.5	6.6	6.4	7.1	7.0	7.2	6.8	7.3	6.7	6.8	7.4	6.7	7.0	5.9	6.0			
1565	6.2	6.1	5.9	6.2	6.3	7.1	6.7	6.1	6.4	6.2	5.9	6.0	5.8	6.2	6.2	5.6	6.4				
1566	7.2	S	7.4	7.3	7.2	7.4	7.1	7.0	7.5	7.2	7.8	7.6	7.2	6.9	7.4	7.4	6.8	6.6	7.3	6.9	
1567	NOT PREGNANT																				
1568	7.3	7.6	7.2	7.1	8.0	7.6	7.6	7.3	7.3	6.5	7.1	7.4	7.8	7.0	6.5						
1569	7.1	D	7.6	7.3	7.1	7.0	7.4	6.6	7.3	7.3	7.0	7.0	6.6	6.7	7.6	6.4	7.5				
1570	7.2	7.4	7.2	7.7	6.9	7.2	7.2	7.6	7.7	7.4	7.2	6.7	6.8	6.9	7.3	6.8	7.2				
1571	7.5	S	8.3	7.3	7.4	8.0	7.3	7.4	7.5	7.7	7.5	8.0	7.4	7.3	7.7	6.5	7.0				
1572	6.8	7.5	6.8	6.5	6.9	7.3	7.0	6.9	5.7	6.7	6.4	7.0	6.8	7.2	7.1	6.7					
1573	7.3	D	8.0	8.0	8.0	7.3	8.2	7.4	7.0	7.3	7.7	6.3	7.4	7.4	7.0	4.8					
1574	7.7	7.8	8.0	7.9	7.7	7.9	8.3	6.9	7.7	7.5	7.9	8.0	7.9	7.6	7.2						
MEAN	7.1																				
S.D.	0.41																				
N	11																				

PUP STATUS CODES: S-STILLBORN D-DIED

6-FEB-2004 10:09

Huntingdon Life Sciences 03-4254

PAGE 279

APPENDIX U - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

GROUP 2		64 MG/KG/DAY															INDIVIDUAL PUP BODY WEIGHTS (GRAMS)					LACTATION DAY 1				
FEMALE#	MEAN	PUP#																								
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19						
2563	6.8	7.5	8.0	6.9	7.2	7.9	6.5	6.7	6.8	6.5	6.4	6.3	6.3	6.5	6.6	6.5	6.4									
2564	8.2	9.1	9.2	8.1	8.4	7.9	8.3	8.6	8.3	7.9	6.7	7.7	8.5	8.0												
2565	7.4	7.8	7.6	7.6	8.1	7.5	7.4	7.5	8.0	6.8	7.4	7.2	7.0	6.8	7.7	7.3										
2566	6.6	6.7	7.0	7.4	6.9	6.0	6.2	6.4	6.4	6.5	6.2	7.0	6.7	6.4												
2567	7.4	7.7	8.0	7.7	7.5	7.6	7.2	7.3	7.2	6.9	7.6	7.2	6.6	7.6												
2568	7.6	D	S	8.1	7.4	7.2	8.2	7.8	8.4	7.5	7.6	7.0	7.7	7.1	7.1	7.5										
2569	7.3	7.2	8.0	7.8	7.1	7.8	7.4	7.2	7.3	7.2	7.1	6.6	7.1	7.6	7.0	7.2										
2570	6.2	6.5	6.1	6.8	6.5	5.8	6.8	6.9	5.9	6.3	5.4	5.8	6.4	6.0	6.0											
2571	8.4	8.6	8.8	9.0	8.4	8.7	8.4	8.2	8.4	8.0	8.6	8.1	8.4	8.0	8.7	7.9	8.2									
2572	NOT PREGNANT																									
2573	8.3	7.1	8.9	8.2	9.1	8.6	8.1	8.4	8.9	7.9	8.9	8.3	8.5	7.6	8.4	8.2										
2574	7.7	8.2	7.8	7.5	7.9	6.7	7.9	7.8	8.1	7.4																
MEAN	7.5																									
S.D.	0.71																									
N	11																									

PUP STATUS CODES: S-STILLBORN D-DIED

6-FEB-2004 10:09

Huntingdon Life Sciences 03-4254

PAGE 280

APPENDIX U - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

GROUP 3		160 MG/KG/DAY																			INDIVIDUAL PUP BODY WEIGHTS (GRAMS)										LACTATION DAY 1				
FEMALE#	MEAN	PUP#																																	
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19															
3563	6.6	6.5	6.5	7.0	6.7	7.3	7.1	6.5	D	6.9	6.8	6.3	6.5	6.1	6.7	5.4	5.9	6.8	6.8	6.3															
3564	7.2	7.0	7.2	8.1	7.3	7.4	7.8	7.0	7.1	7.5	6.8	6.3	7.9	7.3	6.5	6.9																			
3565	6.2	6.5	7.0	6.4	6.4	6.6	6.5	6.4	5.7	5.5	6.4	5.5	5.7	6.3	6.0	6.2																			
3566	7.2	6.7	7.3	7.7	7.5	6.5	7.8	8.1	7.7	7.8	6.1	7.9	6.5	6.6	7.0																				
3567	6.4	6.2	6.5	7.7	7.1	6.0	4.8	6.1	6.1	6.5	6.5	6.0	6.9	6.5	6.3	6.4	6.8																		
3568	7.8	8.0	8.1	8.1	8.4	7.8	8.1	7.6	7.6	8.4	7.4	7.6	7.6	7.4	7.5																				
3569	9.2	S	S	S	8.8	9.5																													
3570	7.0	7.1	7.2	7.5	7.5	7.5	6.8	6.8	6.5	6.4	7.3	6.7																							
3571	8.5	S	8.2	8.4	8.8	9.0	8.5	9.3	9.0	8.1	8.4	7.9	8.8	8.3	8.3	8.5																			
3572	7.5	7.9	8.0	7.5	7.9	7.7	7.0	7.7	7.7	7.9	7.3	6.9	7.2	7.3	7.2	6.9																			
3573	7.2	7.0	7.6	7.3	7.2	7.8	7.3	7.9	7.2	6.3	6.8	6.3	7.2	7.1	7.4	D	7.8																		
3574	7.5	M	7.6	7.9	7.7	7.8	7.6	8.0	8.6	7.5	7.8	8.0	8.2	7.4	3.5																				
MEAN	7.4																																		
S.D.	0.85																																		
N	12																																		

PUP STATUS CODES: S-STILLBORN D-DIED M-MISSING

6-FEB-2004 10:09

Huntingdon Life Sciences 03-4254

PAGE 281

APPENDIX U - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

		INDIVIDUAL PUP BODY WEIGHTS (GRAMS)																LACTATION DAY 1			
GROUP 4	400 MG/KG/DAY																				
FEMALE#	MEAN	PUP#																			
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	
4563	6.6	6.9	6.9	6.6	6.4	7.1	7.0	7.0	6.7	6.6	6.3	6.6	6.3	6.0							
4564	6.8	6.9	6.7	6.5	7.2	7.2	7.2	6.8	7.3	6.8	7.1	6.3	6.7	6.4	6.5	6.6					
4565	6.2	6.6	6.1	6.1	6.4	M	6.2	6.4	6.6	6.7	6.4	4.9	6.0	6.4	5.5	5.9	6.3	6.1	6.1		
4566	8.2	8.5	8.4	7.5	8.2	8.2	8.5	8.8	8.0	8.4	8.6	8.0	8.4	8.1	7.6						
4567	7.4	7.1	7.8	8.3	7.5	7.7	6.8	8.1	7.2	6.3	8.0	7.3	7.3	7.5	7.1	7.4					
4568	7.6	7.7	7.6	7.5	8.0	7.9	8.0	7.3	7.6	8.0	7.1	6.9	7.3	7.6	7.5	7.8	7.3				
4569	7.6	7.7	7.8	7.7	7.8	8.1	8.2	7.1	7.0	7.8	7.5	6.7	S	S	S						
4570	7.5	8.5	8.0	7.2	8.1	7.2	7.6	7.4	6.9	7.0	7.3	7.1	7.5	7.5	7.2	7.9	8.0	7.3	7.2		
4571	9.0	8.9	9.4	9.3	9.4	9.3	9.5	8.8	8.3	8.8	8.7										
4572	7.3	7.5	7.0	7.2	7.2	8.0	7.1	7.0	7.4	7.3	7.5	7.0	7.0	7.2							
4573	8.7	9.0	9.2	9.2	8.8	8.1	8.8	8.2	7.8	8.9	9.7	9.1	8.5	7.3	8.5	9.1					
4574	7.8	8.1	8.4	7.7	8.0	7.9	7.9	7.6	7.6	8.2	7.7	7.0	7.1	S							
MEAN	7.6																				
S.D.	0.82																				
N	12																				

PUP STATUS CODES: S-STILLBORN M-MISSING

APPENDIX U - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

GROUP 5		1000 MG/KG/DAY														INDIVIDUAL PUP BODY WEIGHTS (GRAMS)					LACTATION DAY 1			
FEMALE#	MEAN	PUP#																						
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19				
5563	5.5	Z	S	D	S	S	M	5.2	5.1	M	5.6	5.2	5.5	D	6.4									
5564	6.7	S	7.3	6.4	6.4	6.6	6.3	7.2	6.9	6.4	6.4	6.9	6.8	6.3	6.7									
5565	6.8	6.8	6.8	6.5	7.4	7.3	6.6	7.1	7.2	7.4	6.5	6.5	6.4	6.8	6.8	6.7	6.3	6.8						
5566	6.4	6.4	7.0	7.2	6.8	7.1	6.6	6.1	6.0	6.1	6.7	5.6	5.5	5.8	7.1									
5567	6.1	5.9	6.2	6.2	5.9	5.9	6.1	6.7	5.4	6.0	6.3	6.1	6.3	5.7	6.1	6.2	5.9							
5568	6.5	7.1	6.5	7.5	6.1	6.1	6.1	6.8	5.9	M	6.7	6.0	7.2	6.6	5.8									
5569	6.8	M	7.6	7.2	6.9	7.0	7.7	7.3	5.9	6.8	7.0	6.6	5.4	6.6										
5570	7.0	D	S	7.6	7.9	7.2	7.4	7.1	6.0	6.7	6.2	7.2	6.9											
5571	5.2	S	M	M	5.2	M	D	M	D	M	M	M	M	M	Z	D	D							
5572	NOT PREGNANT																							
5573	5.8	D	D	D	D	D	D	6.3	6.1	5.4	6.9	5.6	5.9	5.9	5.4	4.8								
5574	7.7	D	D	M	8.1	7.3	8.2	7.7	7.2															
MEAN	6.4																							
S.D.	0.72																							
N	11																							

PUP STATUS CODES: S-STILLBORN D-DIED Z-CANNIBALIZED M-MISSING

APPENDIX U - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

GROUP 1		0 MG/KG/DAY														INDIVIDUAL PUP BODY WEIGHTS (GRAMS)					LACTATION DAY 4			
FEMALE#	MEAN	PUP#																						
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19				
1563	10.6	10.5	10.9	11.6	10.8	9.6	10.8	9.5	10.4	10.2	11.6	10.7	10.1	10.4	10.7									
1564	9.3	S	9.8	8.6	9.5	8.6	9.4	9.5	9.6	9.4	D	9.9	9.6	10.0	9.5	8.7	8.7	8.4						
1565	9.0	M	8.9	9.3	9.2	9.4	10.2	9.0	9.6	9.4	8.4	9.1	8.1	9.3	8.5	7.8	9.4							
1566	10.1	S	10.8	10.4	9.6	10.2	9.8	10.2	10.5	10.1	10.9	11.1	9.5	9.7	10.0	9.7	9.4	10.2	10.6	9.7				
1567	NOT PREGNANT																							
1568	10.8	11.3	10.8	10.3	11.6	10.5	11.0	10.7	11.2	10.0	10.8	11.3	11.5	10.8	10.0									
1569	10.7	D	11.2	11.3	10.9	10.2	11.6	9.5	11.1	11.0	10.8	10.5	9.7	10.2	11.0	9.7	11.1							
1570	10.6	10.7	11.7	12.4	9.5	10.2	11.1	11.0	10.7	10.5	10.6	10.5	9.7	10.2	9.6	10.2	10.9							
1571	10.3	S	11.1	10.1	10.4	11.2	10.4	10.1	10.0	10.5	10.3	10.5	9.8	10.0	10.9	9.4	9.4							
1572	9.8	10.5	9.6	9.5	9.4	10.7	10.4	10.0	8.7	9.4	9.2	10.1	10.3	10.5	9.4	9.8								
1573	10.7	D	10.6	11.8	11.6	12.4	11.6	11.3	11.0	11.1	11.0	9.7	11.1	11.0	9.7	6.4								
1574	12.2	13.1	12.3	12.5	12.2	11.8	13.0	11.1	12.4	11.1	12.5	12.9	11.4	M	M									
MEAN	10.4																							
S.D.	0.85																							
N	11																							

PUP STATUS CODES: S-STILLBORN D-DIED M-MISSING

6-FEB-2004 10:09

Huntingdon Life Sciences 03-4254

PAGE 284

APPENDIX U - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

		INDIVIDUAL PUP BODY WEIGHTS (GRAMS)																LACTATION DAY 4		
GROUP 2	64 MG/KG/DAY																			
FEMALE#	MEAN	PUP#																		
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
2563	10.2	11.2	11.5	10.5	10.8	11.7	9.4	10.2	9.9	9.3	10.3	10.0	9.9	9.3	10.0	9.2	9.4			
2564	11.6	12.7	12.6	11.4	12.1	11.6	11.9	12.1	11.6	10.8	9.3	11.1	12.3	11.4						
2565	10.4	11.1	10.5	10.0	10.4	10.7	10.4	9.6	11.4	9.8	11.1	10.3	9.9	9.6	11.1	10.5				
2566	9.6	9.9	9.4	10.8	9.9	8.6	9.2	9.3	9.5	9.5	8.8	10.4	9.8	9.7						
2567	11.0	11.2	11.9	11.0	10.9	10.9	11.1	10.7	10.6	10.4	11.7	11.0	10.2	D						
2568	11.0	D	S	11.9	11.2	10.7	11.0	11.2	11.5	11.4	11.3	10.4	11.1	11.0	10.1	10.7				
2569	9.7	9.5	9.6	10.9	8.9	10.3	9.5	9.4	10.2	9.9	8.9	8.9	9.5	10.0	10.2	9.6				
2570	9.6	10.4	9.5	10.3	9.6	9.4	9.9	10.2	9.3	9.7	8.2	8.7	9.8	9.3	9.4					
2571	11.7	11.6	12.1	12.8	12.5	12.3	11.4	11.5	11.2	11.3	11.8	11.6	11.2	11.5	12.2	11.0	11.5			
2572	NOT PREGNANT																			
2573	11.3	9.7	11.9	11.4	12.3	12.3	11.2	10.9	12.2	10.3	11.8	10.7	11.3	11.3	11.7	11.2				
2574	11.8	12.3	11.5	11.4	12.1	10.2	11.8	13.0	12.1	11.4										
MEAN	10.7																			
S.D.	0.87																			
N	11																			

PUP STATUS CODES: S-STILLBORN D-DIED

6-FEB-2004 10:09

Huntingdon Life Sciences 03-4254

PAGE 285

APPENDIX U - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

		INDIVIDUAL PUP BODY WEIGHTS (GRAMS)															LACTATION DAY 4				
GROUP 3	160 MG/KG/DAY																				
FEMALE#	MEAN	PUP#																			
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	
3563	9.1	8.9	8.5	9.9	9.5	9.8	9.0	9.7	D	9.6	9.8	9.0	8.7	8.5	9.5	7.3	8.0	9.7	9.4	8.8	
3564	9.9	9.9	10.0	11.4	10.3	10.5	10.4	9.9	10.2	10.4	9.6	9.0	10.5	9.8	8.8	8.4					
3565	9.0	9.5	9.3	9.2	9.6	9.6	9.2	9.0	7.8	8.0	9.1	8.5	8.9	9.3	8.7	8.9					
3566	10.9	10.4	11.0	11.6	11.3	9.8	11.2	12.1	11.0	11.7	9.4	11.8	10.3	10.3	10.3						
3567	9.4	9.1	10.0	10.9	9.9	9.4	7.3	9.6	8.1	10.0	9.6	8.8	9.3	9.0	9.3	9.5	9.8				
3568	10.3	10.5	10.9	10.3	11.2	10.6	10.5	9.7	10.2	10.7	10.4	9.4	10.3	10.0	10.0						
3569	13.9	S	S	S	14.1	13.7															
3570	8.8	9.0	8.8	9.3	9.4	9.0	8.5	8.5	8.2	8.6	9.4	8.5									
3571	12.7	S	12.0	13.1	12.3	13.0	13.4	13.3	13.2	12.2	13.1	12.1	12.3	12.6	12.3	12.5					
3572	10.3	10.0	10.7	10.3	10.7	10.8	9.8	10.7	10.8	10.5	10.3	9.8	10.1	10.2	10.2	10.0					
3573	10.8	10.7	11.6	10.4	10.7	11.4	10.9	11.1	11.0	10.0	10.1	10.1	11.2	10.4	10.9	D	11.3				
3574	11.8	M	12.3	12.8	12.0	12.9	11.4	12.3	13.6	12.1	12.4	12.4	12.3	11.3	5.4						
MEAN	10.6																				
S.D.	1.56																				
N	12																				

PUP STATUS CODES: S-STILLBORN D-DIED M-MISSING

APPENDIX U - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

		INDIVIDUAL PUP BODY WEIGHTS (GRAMS)																		LACTATION DAY 4	
GROUP 4	400 MG/KG/DAY																				
FEMALE#	MEAN	PUP#																			
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	
4563	9.6	9.9	9.5	9.4	9.1	9.7	9.5	10.2	10.1	9.4	9.9	9.7	8.9	9.0							
4564	8.0	8.3	7.8	7.8	8.3	8.6	8.4	8.1	8.5	8.0	8.3	7.6	7.9	7.6	7.8	7.6					
4565	8.6	9.3	8.8	8.4	9.0	M	7.9	9.2	9.6	9.1	9.8	6.3	8.7	8.3	7.7	8.6	8.9	9.0	8.4		
4566	11.6	12.3	11.5	10.7	11.7	12.0	11.8	11.9	11.2	11.8	11.9	11.5	12.3	11.2	10.4						
4567	10.6	10.5	10.7	10.2	11.3	9.9	10.3	12.2	10.8	10.2	11.6	10.5	10.0	9.3	9.8	11.0					
4568	10.5	11.2	10.6	10.4	11.5	10.8	10.5	9.6	10.5	10.5	11.3	9.5	10.3	9.4	10.3	10.8	10.3				
4569	11.0	10.8	10.9	11.1	11.1	11.6	11.8	10.3	10.4	11.5	11.1	10.5	S	S	S						
4570	10.1	11.7	10.6	10.7	10.6	9.4	9.9	10.6	9.9	8.4	9.4	10.1	9.1	9.9	9.6	10.7	11.1	10.2	9.1		
4571	13.5	12.9	14.1	14.2	14.2	13.6	13.7	13.5	12.5	12.7	13.5										
4572	11.0	10.2	11.2	10.3	11.4	11.9	10.3	11.3	11.3	11.8	10.8	10.7	11.4	10.8							
4573	12.5	12.6	13.5	13.0	12.9	11.9	12.3	11.3	11.8	12.8	13.5	12.9	11.9	10.7	13.1	12.8					
4574	10.9	11.1	11.1	10.5	11.5	11.5	11.6	11.0	10.7	11.0	10.6	9.9	10.5	S							
MEAN	10.7																				
S.D.	1.51																				
N	12																				

PUP STATUS CODES: S-STILLBORN M-MISSING

APPENDIX U - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

GROUP 5		1000 MG/KG/DAY														INDIVIDUAL PUP BODY WEIGHTS. (GRAMS)					LACTATION DAY 4			
FEMALE#	MEAN	PUP#																						
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19				
5563	7.6	Z	S	D	S	S	M	D	7.2	M	7.5	7.0	7.4	D	9.0									
5564	9.2	S	9.6	9.5	9.3	9.1	8.8	9.6	9.2	9.3	8.8	9.3	9.3	8.7	8.9									
5565	8.1	7.8	7.9	8.0	8.8	9.0	8.0	8.3	8.6	8.8	7.9	8.2	7.4	7.9	D	8.8	7.1	7.3						
5566	8.9	9.1	10.1	9.3	9.7	9.5	8.7	8.6	8.7	9.2	9.0	8.0	7.4	8.2	9.6									
5567	8.2	8.0	8.3	8.1	8.4	8.0	8.4	8.7	7.8	7.9	7.8	8.3	8.6	7.9	8.4	8.6	8.1							
5568	10.0	10.0	10.2	11.3	9.9	9.2	9.2	10.5	9.9	M	10.8	9.2	10.7	9.9	8.6									
5569	10.2	M	11.1	10.8	10.5	10.8	10.9	10.8	9.5	9.8	9.8	10.2	8.3	9.9										
5570	10.4	D	S	10.3	11.4	10.7	10.4	10.5	D	10.5	9.4	10.4	9.9											
5571	TOTAL LITTER LOSS																							
5572	NOT PREGNANT																							
5573	6.6	D	D	D	D	D	D	4.3	7.4	6.7	8.0	D	7.4	D	5.9	D								
5574	11.7	D	D	M	11.4	11.0	12.4	12.0	11.7															
MEAN	9.1																							
S.D.	1.51																							
N	10																							

PUP STATUS CODES: S-STILLBORN D-DIED Z-CANNIBALIZED M-MISSING

APPENDIX U - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

GROUP 1		0 MG/KG/DAY																			INDIVIDUAL PUP BODY WEIGHTS (GRAMS)										LACTATION DAY 7				
FEMALE#	MEAN	PUP#																																	
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19															
1563	17.0	C	18.5	17.6	C	15.6	17.2	15.3	16.9	16.6	18.1	C	16.4	C	17.4																				
1564	15.2	S	C	C	15.7	14.5	15.9	15.7	C	C	D	16.2	15.8	C	15.5	14.2	15.0	13.7																	
1565	15.1	M	15.0	15.4	C	C	16.4	15.0	16.1	16.0	13.7	C	14.4	C	C	12.8	15.8																		
1566	15.9	S	16.9	C	C	16.6	16.0	C	C	C	C	C	15.3	15.5	15.6	15.9	15.3	C	16.8	15.2															
1567	NOT PREGNANT																																		
1568	17.0	C	C	16.3	18.3	16.9	18.2	16.7	C	15.7	16.9	17.6	C	17.1	16.2																				
1569	17.4	D	18.8	18.2	17.5	17.7	18.3	15.5	C	C	C	C	15.5	16.2	18.0	C	18.6																		
1570	17.3	C	C	18.9	16.7	16.9	C	18.0	C	C	17.8	C	16.1	17.3	16.8	16.7	18.0																		
1571	16.5	S	C	17.0	16.5	C	16.9	C	C	16.6	16.6	C	15.4	16.8	17.5	15.9	15.4																		
1572	15.9	17.0	15.4	15.8	C	17.4	C	15.6	14.4	15.2	C	16.5	16.8	C	14.8	C																			
1573	16.7	D	17.0	C	17.9	19.2	18.4	C	17.6	C	C	15.6	16.8	17.8	16.3	10.4																			
1574	19.1	20.1	19.0	C	20.2	19.2	C	17.1	18.6	17.9	19.5	20.6	18.4	M	M																				
MEAN	16.6																																		
S.D.	1.13																																		
N	11																																		

PUP STATUS CODES: S-STILLBORN D-DIED C-CULLED M-MISSING

APPENDIX U - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

		INDIVIDUAL PUP BODY WEIGHTS (GRAMS)															LACTATION DAY 7			
GROUP 2	64 MG/KG/DAY																			
FEMALE#	MEAN	PUP#																		
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
2563	17.5	19.5	19.5	C	18.7	19.4	16.0	C	C	16.0	C	16.9	17.1	15.6	C	C	16.4			
2564	18.1	19.1	20.1	17.4	18.1	18.4	18.5	18.3	C	C	14.6	C	18.6	17.7						
2565	16.5	17.0	16.6	16.0	C	17.1	C	C	C	C	17.9	16.6	15.3	15.5	17.4	15.8				
2566	14.8	15.0	14.4	16.7	14.5	C	14.4	14.5	C	C	13.5	15.4	15.2	14.5						
2567	16.4	C	17.7	16.9	16.5	16.8	16.8	14.2	C	16.2	17.2	16.7	15.3	D						
2568	17.5	D	S	18.4	17.5	16.9	18.1	18.2	18.1	C	C	C	17.7	16.9	16.2	16.9				
2569	15.9	C	15.4	17.0	14.5	16.6	15.9	16.3	16.4	C	C	C	15.3	16.3	C	15.0				
2570	14.9	16.2	14.8	15.7	15.4	14.9	C	C	14.4	15.6	13.0	13.6	C	C	14.9					
2571	19.8	20.3	C	20.9	C	C	C	19.4	19.7	19.8	20.0	19.3	C	19.1	19.5	C	19.6			
2572	NOT PREGNANT																			
2573	18.7	C	C	C	19.8	19.2	18.3	C	19.5	C	19.0	17.8	18.2	18.0	18.6	18.3				
2574	17.3	17.4	17.2	17.2	17.9	14.7	17.6	18.8	17.4	17.1										
MEAN	17.0																			
S.D.	1.53																			
N	11																			

PUP STATUS CODES: S-STILLBORN D-DIED C-CULLED

APPENDIX U - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

GROUP 3		160 MG/KG/DAY															INDIVIDUAL PUP BODY WEIGHTS (GRAMS).					LACTATION DAY 7				
FEMALE#	MEAN	PUP#																								
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19						
3563	15.8	C	14.9	C	C	16.5	16.0	16.4	D	16.5	C	C	15.6	14.9	C	C	C	16.3	16.2	15.0						
3564	16.0	C	15.5	17.3	16.4	16.9	16.5	C	15.7	16.3	15.3	14.5	16.1	C	C	C										
3565	13.9	14.3	14.2	14.4	14.3	C	14.0	C	C	12.2	14.1	C	13.8	14.2	13.4	C										
3566	17.2	C	16.8	18.6	17.4	C	17.8	C	C	18.3	15.2	19.0	16.1	16.6	16.6											
3567	15.0	15.1	16.3	17.1	16.4	C	10.7	15.4	13.6	15.6	C	14.6	15.5	C	C	C	C									
3568	16.2	C	16.6	16.2	16.9	16.5	C	15.6	C	C	15.6	15.6	16.6	16.4	16.1											
3569	20.8	S	S	S	20.7	20.9																				
3570	12.7	12.8	12.4	13.3	13.7	13.0	12.3	12.6	11.9	C	13.0	12.1														
3571	20.4	S	19.7	21.2	19.9	C	21.1	21.0	21.6	19.3	20.4	C	20.1	C	C	20.0										
3572	17.0	17.5	17.8	17.3	C	C	16.5	C	C	17.0	17.0	C	17.2	16.5	16.6	16.4										
3573	16.2	15.5	17.1	16.0	16.8	16.6	C	16.6	17.1	14.8	C	15.3	C	15.8	C	D	C									
3574	18.6	M	19.3	20.4	C	20.2	18.7	19.6	C	19.7	19.6	20.0	19.4	C	9.0											
MEAN	16.7																									
S.D.	2.39																									
N	12																									

PUP STATUS CODES: S-STILLBORN D-DIED C-CULLED M-MISSING

APPENDIX U - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

		INDIVIDUAL PUP BODY WEIGHTS (GRAMS)														LACTATION DAY 7				
GROUP 4	400 MG/KG/DAY																			
FEMALE#	MEAN	PUP#																		
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
4563	15.2	16.5	16.0	14.7	C	C	14.6	16.2	15.8	15.7	C	15.5	14.1	13.3						
4564	12.7	12.9	12.4	12.8	C	13.4	C	12.7	C	12.4	13.1	12.2	12.6	C	12.2	C				
4565	13.7	C	C	13.9	14.6	M	C	C	C	15.1	C	10.5	13.8	14.1	13.2	13.5	14.9	C	13.5	
4566	17.7	C	17.2	17.3	C	18.4	18.0	18.9	17.6	C	C	17.8	18.2	17.5	16.5					
4567	16.4	15.7	16.3	C	C	C	C	18.0	16.8	16.0	16.7	16.3	16.0	16.4	16.1	C				
4568	16.7	C	C	15.9	17.7	17.1	16.7	C	C	17.1	16.9	C	17.1	15.6	15.7	17.1	C			
4569	17.5	17.0	C	17.7	17.8	18.4	18.3	16.8	16.3	18.2	18.0	16.9	S	S	S					
4570	16.7	C	17.3	17.9	17.9	15.9	17.6	C	16.7	13.9	15.3	C	C	16.9	C	C	C	17.6	C	
4571	18.8	18.3	19.1	19.6	19.4	18.8	19.6	18.5	17.7	18.1	18.6									
4572	17.6	17.0	17.4	17.0	18.2	18.1	16.6	17.7	17.5	18.6	C	C	C	17.9						
4573	19.5	C	C	C	C	18.9	19.2	18.3	19.5	C	21.7	20.3	18.4	17.4	20.5	20.4				
4574	17.0	17.0	17.6	16.2	17.0	17.7	17.3	C	16.4	17.7	16.5	C	16.6	S						
MEAN	16.6																			
S.D.	1.95																			
N	12																			

PUP STATUS CODES: S-STILLBORN C-CULLED M-MISSING

APPENDIX U - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

GROUP 5		1000 MG/KG/DAY														INDIVIDUAL PUP BODY WEIGHTS (GRAMS)										LACTATION DAY 7			
FEMALE#	MEAN	PUP#																											
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19									
5563	13.2	Z	S	D	S	S	M	D	12.4	M	13.3	12.2	12.9	D	15.4														
5564	13.7	S	14.4	14.5	13.2	13.8	13.1	C	C	C	13.6	14.1	13.9	13.1	13.7														
5565	11.5	11.4	11.3	C	12.6	C	11.3	C	C	12.3	11.3	11.5	C	11.1	D	11.7	C	10.7											
5566	13.5	C	15.0	14.7	14.5	C	13.6	13.2	C	C	13.6	11.8	11.1	13.0	14.4														
5567	13.3	13.0	13.1	13.3	13.4	C	C	C	13.1	13.0	C	C	14.0	12.8	C	13.6	13.2												
5568	14.7	C	14.5	16.4	14.8	13.3	C	15.3	14.9	M	14.7	13.6	15.3	14.2	C														
5569	16.1	M	17.4	16.9	C	16.6	18.1	C	15.6	15.5	15.4	16.3	13.0	16.0															
5570	14.9	D	S	14.5	15.7	15.4	15.5	14.8	D	15.2	13.6	15.1	14.5																
5571	TOTAL LITTER LOSS																												
5572	NOT PREGNANT																												
5573	11.1	D	D	D	D	D	D	D	11.6	10.2	12.6	D	11.4	D	9.5	D													
5574	18.1	D	D	M	18.2	17.4	18.7	18.4	17.9																				
MEAN	14.0																												
S.D.	2.08																												
N	10																												

PUP STATUS CODES: S-STILLBORN D-DIED C-CULLED Z-CANNIBALIZED M-MISSING

APPENDIX U - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

GROUP 1		0 MG/KG/DAY														INDIVIDUAL PUP BODY WEIGHTS (GRAMS)				LACTATION DAY 14			
FEMALE#	MEAN		PUP#																				
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19		
1563	33.2	C	34.7	33.8	C	31.7	33.5	33.0	32.9	32.3	35.5	C	32.2	C	32.8								
1564	29.6	S	C	C	31.0	28.7	30.1	31.0	C	C	D	31.3	31.7	C	29.4	27.7	28.4	27.0					
1565	32.4	M	32.6	35.3	C	C	35.7	33.3	34.6	32.7	29.6	C	29.4	C	C	28.5	32.2						
1566	33.7	S	32.6	C	C	35.0	35.3	C	C	C	C	C	33.1	34.5	33.1	32.3	33.1	C	34.4	33.9			
1567	NOT PREGNANT																						
1568	31.6	C	C	31.6	34.4	31.5	32.7	30.3	C	30.4	31.9	32.1	C	31.1	30.2								
1569	33.9	D	37.2	35.8	36.5	33.8	35.1	30.5	C	C	C	C	31.1	30.6	33.9	C	34.2						
1570	34.8	C	C	34.9	33.7	35.2	C	35.9	C	C	36.3	C	33.6	33.4	33.6	35.6	36.1						
1571	32.1	S	C	32.3	32.0	C	32.8	C	C	32.4	32.2	C	31.4	31.7	33.4	31.7	30.7						
1572	29.1	29.9	28.3	29.2	C	31.5	C	28.6	27.0	28.6	C	30.2	30.0	C	27.9	C							
1573	33.0	D	35.2	C	34.0	36.4	34.7	C	33.8	C	C	33.5	33.9	34.2	31.1	23.5							
1574	34.8	34.6	34.8	C	36.3	35.0	C	32.1	34.5	33.5	35.4	36.1	35.3	M	M								
MEAN	32.6																						
S.D.	1.88																						
N	11																						

PUP STATUS CODES: S-STILLBORN D-DIED C-CULLED M-MISSING

APPENDIX U - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

		INDIVIDUAL PUP BODY WEIGHTS (GRAMS)																		LACTATION DAY 14	
GROUP 2	64 MG/KG/DAY																				
FEMALE#	MEAN	PUP#																			
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	
2563	34.9	37.8	36.2	C	36.1	38.7	34.2	C	C	33.0	C	34.0	33.8	33.3	C	C	31.6				
2564	34.2	35.0	36.4	34.8	34.2	34.6	34.0	34.0	C	C	30.4	C	34.7	34.1							
2565	32.6	33.8	31.8	32.0	C	32.9	C	C	C	C	34.6	33.1	30.6	31.7	33.6	32.2					
2566	27.1	28.0	26.3	30.0	26.8	C	27.1	25.9	C	C	26.0	27.5	25.7	27.3							
2567	28.9	C	29.4	29.5	27.8	29.4	30.4	27.3	C	28.5	29.1	28.6	28.5	D							
2568	30.7	D	S	32.3	30.1	30.6	31.9	33.2	30.2	C	C	C	29.7	30.6	28.2	30.2					
2569	31.2	C	29.8	33.3	29.6	32.6	32.5	32.0	30.7	C	C	C	31.1	31.5	C	28.9					
2570	31.1	33.1	31.7	33.2	31.3	32.0	C	C	30.1	30.9	28.3	30.5	C	C	29.5						
2571	37.8	39.0	C	39.4	C	C	C	38.0	37.8	37.8	36.1	36.6	C	37.8	38.2	C	37.8				
2572	NOT PREGNANT																				
2573	32.8	C	C	C	34.2	34.5	33.7	C	32.7	C	31.8	33.7	31.0	31.3	32.9	32.4					
2574	30.7	31.2	29.6	30.0	31.2	28.0	31.1	33.3	30.3	31.4											
MEAN	32.0																				
S.D.	2.96																				
N	11																				

PUP STATUS CODES: S-STILLBORN D-DIED C-CULLED

APPENDIX U - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

GROUP 3		160 MG/KG/DAY														INDIVIDUAL PUP BODY WEIGHTS (GRAMS)						LACTATION DAY 14				
FEMALE#	MEAN	PUP#																								
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19						
3563	30.9	C	29.7	C	C	31.7	31.1	32.3	D	32.2	C	C	30.5	29.1	C	C	C	C	32.5	31.2	29.1					
3564	30.4	C	29.8	33.1	30.0	31.3	31.3	C	29.5	31.1	28.6	27.3	32.3	C	C	C										
3565	29.4	30.2	28.7	29.2	30.0	C	30.1	C	C	26.8	30.0	C	30.0	29.7	29.7	C										
3566	27.4	C	27.6	29.0	26.6	C	29.4	C	C	27.0	24.6	29.4	27.3	25.9	27.0											
3567	30.2	29.9	32.6	31.8	32.9	C	25.2	30.0	28.3	29.5	C	30.3	31.6	C	C	C	C									
3568	30.5	C	31.1	30.5	31.0	32.0	C	29.3	C	C	31.1	29.8	30.5	30.0	30.1											
3569	40.1	S	S	S	40.2	39.9																				
3570	24.9	25.0	24.2	26.1	26.6	25.4	25.0	23.7	24.4	C	25.5	23.5														
3571	36.7	S	37.7	37.4	36.9	C	36.9	36.9	38.7	34.6	36.2	C	36.4	C	C	35.0										
3572	31.9	33.0	32.4	33.2	C	C	29.4	C	C	31.9	32.7	C	32.2	32.4	29.7	31.6										
3573	32.5	31.5	33.8	32.7	32.2	33.4	C	33.4	33.5	30.2	C	32.9	C	31.8	C	D	C	C								
3574	35.0	M	36.0	37.1	C	38.2	35.0	36.5	C	37.1	35.8	36.3	36.5	C	21.1											
MEAN	31.7																									
S.D.	4.06																									
N	12																									

PUP STATUS CODES: S-STILLBORN D-DIED C-CULLED M-MISSING

APPENDIX U - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

		INDIVIDUAL PUP BODY WEIGHTS (GRAMS)																		LACTATION DAY 14	
GROUP 4	400 MG/KG/DAY																				
FEMALE#	MEAN	PUP#																			
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	
4563	31.7	34.3	32.8	31.4	C	C	32.0	30.9	31.9	32.9	C	32.4	31.0	27.5							
4564	25.5	25.6	25.8	26.8	C	25.9	C	26.4	C	24.4	25.5	25.7	24.6	C	24.6	C					
4565	27.5	C	C	27.4	29.5	M	C	C	C	29.5	C	22.9	27.8	28.0	26.5	27.4	29.1	C	27.4		
4566	35.2	C	D	34.6	C	35.6	35.8	38.0	34.6	C	C	35.6	35.0	33.5	34.3						
4567	30.8	29.7	28.6	C	C	C	C	32.8	33.2	32.2	30.4	29.9	31.3	28.6	31.5	C					
4568	32.7	C	C	32.5	34.7	33.7	32.7	C	C	34.4	32.0	C	32.5	31.8	31.0	31.8	C				
4569	31.9	32.3	C	32.3	32.4	32.9	32.0	30.6	31.0	33.2	32.1	30.2	S	S	S						
4570	32.9	C	32.8	33.8	34.6	33.1	34.7	C	33.2	29.3	31.3	C	C	31.8	C	C	C	34.0	C		
4571	33.5	33.5	34.2	34.9	34.2	33.8	34.3	32.9	31.2	32.4	33.3										
4572	34.8	34.3	34.0	34.5	35.6	35.1	33.5	34.1	35.2	35.6	C	C	C	36.5							
4573	37.1	C	C	C	C	37.6	37.8	36.9	35.7	C	39.1	37.5	37.0	34.3	37.2	37.7					
4574	31.7	32.3	33.5	30.9	32.0	33.9	30.4	C	29.2	32.6	31.4	C	31.2	S							
MEAN	32.1																				
S.D.	3.17																				
N	12																				

PUP STATUS CODES: S-STILLBORN D-DIED C-CULLED M-MISSING

6-FEB-2004 10:09

Huntingdon Life Sciences 03-4254

PAGE 297

APPENDIX U - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

GROUP 5		1000 MG/KG/DAY														INDIVIDUAL PUP BODY WEIGHTS (GRAMS)						LACTATION DAY 14			
FEMALE#	MEAN	PUP#																							
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19					
5563	30.8	Z	S	D	S	S	M	D	29.9	M	29.9	30.7	30.8	D	32.9										
5564	26.6	S	27.6	28.8	26.2	27.4	26.0	C	C	C	25.9	26.6	26.3	24.6	26.9										
5565	22.9	22.7	23.7	C	23.6	C	23.5	C	C	23.5	21.6	23.3	C	22.2	D	23.3	C	21.7							
5566	26.3	C	28.1	27.8	27.6	C	27.7	26.3	C	C	25.8	22.8	23.8	25.5	27.2										
5567	25.9	25.7	26.0	26.1	24.8	C	C	C	26.5	24.7	C	C	26.4	25.2	C	27.3	25.8								
5568	28.6	C	29.3	31.7	26.6	28.2	C	30.4	30.0	M	27.6	27.6	27.7	27.2	C										
5569	31.4	M	33.8	32.4	C	32.1	34.1	C	31.8	30.5	29.7	31.1	27.2	31.7											
5570	27.6	D	S	26.3	29.1	28.7	27.5	26.6	D	27.4	25.8	29.2	28.0												
5571	TOTAL LITTER LOSS																								
5572	NOT PREGNANT																								
5573	20.9	D	D	D	D	D	D	D	20.9	20.5	22.3	D	21.6	D	19.1	D									
5574	34.2	D	D	M	34.6	32.6	34.9	33.6	35.2																
MEAN	27.5																								
S.D.	3.98																								
N	10																								

PUP STATUS CODES: S-STILLBORN D-DIED C-CULLED Z-CANNIBALIZED M-MISSING

APPENDIX U - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

GROUP 1		0 MG/KG/DAY																			INDIVIDUAL PUP BODY WEIGHTS (GRAMS)																			LACTATION DAY 21																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																							
FEMALE#	MEAN	PUP#																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																													
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																											
1563	52.2	C	52.9	56.6	C	50.2	55.9	50.9	53.3	49.1	52.7	C	48.5	C	51.7																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																

PUP STATUS CODES: S-STILLBORN D-DIED C-CULLED M-MISSING

APPENDIX U - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

		INDIVIDUAL PUP BODY WEIGHTS (GRAMS)																			
GROUP 2	64 MG/KG/DAY																			LACTATION DAY 21	
FEMALE#	MEAN	PUP#																			
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	
2563	52.9	57.0	55.4	C	52.0	57.0	51.0	C	C	50.1	C	52.5	50.7	55.1	C	C	48.2				
2564	56.4	59.0	59.3	57.3	57.4	58.0	54.8	53.5	C	C	50.3	C	56.4	57.6							
2565	54.4	56.6	53.5	54.1	C	53.3	C	C	C	C	58.7	55.1	52.8	51.1	56.0	52.8					
2566	44.7	45.5	44.9	52.6	44.0	C	44.8	43.4	C	C	41.8	44.2	41.5	44.5							
2567	48.9	C	49.3	49.6	50.4	53.0	50.8	44.4	C	49.7	48.9	46.1	47.0	D							
2568	52.8	D	S	54.2	54.8	51.9	50.3	59.0	52.5	C	C	C	52.3	53.8	47.1	52.1					
2569	52.2	C	52.5	59.0	49.5	54.3	53.0	50.9	50.6	C	C	C	51.8	51.2	C	49.5					
2570	49.0	49.8	49.3	55.2	48.2	52.7	C	C	48.6	48.4	42.2	46.0	C	C	49.5						
2571	64.0	65.8	C	64.6	C	C	C	65.5	65.0	61.4	62.2	58.8	C	68.9	62.8	C	64.7				
2572	NOT PREGNANT																				
2573	55.3	C	C	C	57.9	59.5	56.2	C	55.5	C	55.5	57.0	51.4	52.6	53.6	54.3					
2574	52.0	52.7	51.8	51.1	53.4	46.7	53.1	56.1	51.1	51.7											
MEAN	53.0																				
S.D.	4.92																				
N	11																				

PUP STATUS CODES: S-STILLBORN D-DIED C-CULLED

APPENDIX U - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

GROUP 3		160 MG/KG/DAY														INDIVIDUAL PUP BODY WEIGHTS (GRAMS)					LACTATION DAY 21				
FEMALE#	MEAN	PUP#																							
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19					
3563	52.2	C	50.5	C	C	55.0	52.1	57.0	D	52.2	C	C	49.7	50.1	C	C	C	55.8	52.7	46.8					
3564	52.4	C	52.9	57.2	54.4	52.4	55.6	C	47.6	52.9	51.7	46.5	52.7	C	C	C									
3565	48.0	47.2	50.0	48.4	50.2	C	49.1	C	C	42.0	50.6	C	46.9	46.2	49.8	C									
3566	43.6	C	42.6	44.2	43.6	C	46.8	C	C	45.6	37.2	50.0	41.2	43.1	41.9										
3567	50.7	47.1	55.9	53.6	58.0	C	42.9	51.1	47.0	51.5	C	50.3	49.9	C	C	C	C								
3568	51.7	C	54.3	52.9	52.5	56.2	C	49.6	C	C	52.2	47.9	50.5	50.4	50.0										
3569	64.0	S	S	S	64.5	63.5																			
3570	41.1	42.4	38.0	40.2	42.5	41.9	40.0	42.1	40.3	C	42.0	41.2													
3571	64.7	S	66.4	65.5	68.3	C	65.2	64.6	66.1	65.8	63.0	C	63.6	C	C	58.0									
3572	55.1	56.3	55.5	56.4	C	C	50.0	C	C	57.2	56.7	C	53.5	54.3	54.1	56.5									
3573	56.4	54.4	57.1	56.3	55.8	57.5	C	59.6	57.9	53.9	C	57.3	C	53.9	C	D	C	C							
3574	54.3	M	54.3	59.2	C	59.5	53.6	57.3	C	57.5	55.3	57.8	55.7	C	33.0										
MEAN	52.8																								
S.D.	6.99																								
N	12																								

PUP STATUS CODES: S-STILLBORN D-DIED C-CULLED M-MISSING

APPENDIX U - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

		INDIVIDUAL PUP BODY WEIGHTS (GRAMS)																			LACTATION DAY 21	
GROUP 4	400 MG/KG/DAY																					
FEMALE#	MEAN	PUP#																				
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19		
4563	50.2	51.1	51.0	48.5	C	C	49.4	50.9	54.7	51.8	C	52.4	47.8	44.8								
4564	43.9	44.4	47.3	44.5	C	45.6	C	45.3	C	43.6	43.5	41.8	41.1	C	41.7	C						
4565	45.7	C	C	45.5	50.3	M	C	C	C	49.2	C	37.2	45.4	47.4	42.1	45.2	49.4	C	45.1			
4566	59.9	C	D	60.9	C	60.1	64.2	66.1	59.5	C	C	63.6	51.2	57.3	56.3							
4567	51.0	49.7	51.3	C	C	C	C	56.6	49.7	47.5	50.5	42.7	54.6	52.5	54.4	C						
4568	53.5	C	C	55.1	59.4	54.5	52.6	C	C	57.4	50.5	C	51.5	51.3	50.4	52.1	C					
4569	51.7	46.9	C	53.3	52.2	52.0	52.0	54.0	52.1	52.7	51.2	50.8	S	S	S							
4570	57.3	C	60.6	60.3	61.8	57.3	59.7	C	53.9	50.8	54.6	C	C	55.4	C	C	C	58.4	C			
4571	59.8	59.6	61.2	65.7	59.2	60.7	63.0	59.1	56.2	55.6	57.4											
4572	56.5	57.3	57.7	59.9	58.7	55.5	51.1	56.3	51.1	58.9	C	C	C	58.6								
4573	62.6	C	C	C	C	62.9	64.3	61.7	59.8	C	68.0	63.7	60.2	58.8	62.6	63.7						
4574	51.0	51.0	53.8	49.9	50.9	55.8	49.4	C	45.7	51.9	51.6	C	50.2	S								
MEAN	53.6																					
S.D.	5.77																					
N	12																					

PUP STATUS CODES: S-STILLBORN D-DIED C-CULLED M-MISSING

APPENDIX U - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

GROUP 5		1000 MG/KG/DAY														INDIVIDUAL PUP BODY WEIGHTS (GRAMS)					LACTATION DAY 21			
FEMALE#	MEAN	PUP#																						
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19				
5563	55.5	Z	S	D	S	S	M	D	56.1	M	55.1	53.9	55.6	D	57.0									
5564	47.2	S	47.9	49.6	48.2	48.0	47.7	C	C	C	47.3	46.8	45.1	45.3	46.6									
5565	40.8	41.1	41.9	C	42.4	C	42.2	C	C	41.3	40.1	41.1	C	38.1	D	40.9	C	39.0						
5566	44.8	C	49.7	44.1	43.4	C	47.4	48.8	C	C	46.0	42.3	38.5	45.1	42.4									
5567	46.6	47.6	46.4	46.2	46.7	C	C	C	44.0	45.0	C	C	48.5	44.7	C	48.9	48.1							
5568	49.4	C	53.2	56.8	45.9	47.8	C	50.9	50.2	M	48.5	44.7	49.8	46.6	C									
5569	54.0	M	55.8	54.9	C	53.8	61.4	C	53.0	53.2	53.1	53.0	47.7	54.3										
5570	46.3	D	S	46.2	50.0	47.6	46.7	44.1	D	46.1	43.5	45.7	46.5											
5571	TOTAL LITTER LOSS																							
5572	NOT PREGNANT																							
5573	42.2	D	D	D	D	D	D	D	42.4	42.4	43.5	D	42.0	D	40.9	D								
5574	60.5	D	D	M	63.1	55.7	61.3	59.7	62.7															
MEAN	48.7																							
S.D.	6.21																							
N	10																							

PUP STATUS CODES: S-STILLBORN D-DIED C-CULLED Z-CANNIBALIZED M-MISSING

6-FEB-2004 10:21

Huntingdon Life Sciences 03-4254P

PAGE 303

APPENDIX V - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL ANIMAL TERMINATION HISTORY

MALES GROUP 1 0 MG/KG/DAY

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY
1075	TERMINAL SACRIFICE	4-SEP-03	28
1076	TERMINAL SACRIFICE	10-SEP-03	28
1077	TERMINAL SACRIFICE	4-SEP-03	28
1078	TERMINAL SACRIFICE	6-SEP-03	28
1079	TERMINAL SACRIFICE	4-SEP-03	28
1080	TERMINAL SACRIFICE	5-SEP-03	28
1081	TERMINAL SACRIFICE	4-SEP-03	28
1082	TERMINAL SACRIFICE	6-SEP-03	28
1083	TERMINAL SACRIFICE	7-SEP-03	28
1084	TERMINAL SACRIFICE	4-SEP-03	28
1085	TERMINAL SACRIFICE	6-SEP-03	28

6-FEB-2004 10:21

Huntingdon Life Sciences 03-4254P

PAGE 304

APPENDIX V - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL ANIMAL TERMINATION HISTORY

MALES GROUP 2 64 MG/KG/DAY

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY
2075	TERMINAL SACRIFICE	5-SEP-03	28
2076	TERMINAL SACRIFICE	9-SEP-03	28
2077	TERMINAL SACRIFICE	4-SEP-03	28
2078	TERMINAL SACRIFICE	3-SEP-03	28
2079	TERMINAL SACRIFICE	7-SEP-03	28
2080	TERMINAL SACRIFICE	7-SEP-03	28
2081	TERMINAL SACRIFICE	6-SEP-03	28
2082	TERMINAL SACRIFICE	3-SEP-03	28
2083	TERMINAL SACRIFICE	7-SEP-03	28
2084	TERMINAL SACRIFICE	5-SEP-03	28
2085	TERMINAL SACRIFICE	6-SEP-03	28

6-FEB-2004 10:21

Huntingdon Life Sciences 03-4254P

PAGE 305

APPENDIX V - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL ANIMAL TERMINATION HISTORY

MALES GROUP 3 160 MG/KG/DAY

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY
3075	TERMINAL SACRIFICE	5-SEP-03	28
3076	TERMINAL SACRIFICE	4-SEP-03	28
3077	TERMINAL SACRIFICE	12-SEP-03	28
3078	TERMINAL SACRIFICE	8-SEP-03	28
3079	TERMINAL SACRIFICE	4-SEP-03	28
3080	TERMINAL SACRIFICE	5-SEP-03	28
3081	TERMINAL SACRIFICE	7-SEP-03	28
3082	TERMINAL SACRIFICE	7-SEP-03	28
3083	TERMINAL SACRIFICE	5-SEP-03	28
3084	TERMINAL SACRIFICE	8-SEP-03	28
3085	TERMINAL SACRIFICE	4-SEP-03	28

6-FEB-2004 10:21

Huntingdon Life Sciences 03-4254P

PAGE 306

APPENDIX V - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL ANIMAL TERMINATION HISTORY

MALES GROUP 4 400 MG/KG/DAY

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY
4075	TERMINAL SACRIFICE	5-SEP-03	28
4076	TERMINAL SACRIFICE	7-SEP-03	28
4077	TERMINAL SACRIFICE	6-SEP-03	28
4078	TERMINAL SACRIFICE	7-SEP-03	28
4079	TERMINAL SACRIFICE	7-SEP-03	28
4080	TERMINAL SACRIFICE	8-SEP-03	28
4081	TERMINAL SACRIFICE	5-SEP-03	28
4082	TERMINAL SACRIFICE	7-SEP-03	28
4083	TERMINAL SACRIFICE	7-SEP-03	28
4084	TERMINAL SACRIFICE	7-SEP-03	28
4085	TERMINAL SACRIFICE	6-SEP-03	28
4086	TERMINAL SACRIFICE	7-SEP-03	28

6-FEB-2004 10:21

Huntingdon Life Sciences 03-4254P

PAGE 307

APPENDIX V - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL ANIMAL TERMINATION HISTORY

MALES GROUP 5 1000 MG/KG/DAY

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY
5075	TERMINAL SACRIFICE	5-SEP-03	28
5076	TERMINAL SACRIFICE	8-SEP-03	28
5077	TERMINAL SACRIFICE	9-SEP-03	28
5078	TERMINAL SACRIFICE	7-SEP-03	28
5079	TERMINAL SACRIFICE	6-SEP-03	28
5080	TERMINAL SACRIFICE	7-SEP-03	28
5081	TERMINAL SACRIFICE	4-SEP-03	28
5082	TERMINAL SACRIFICE	7-SEP-03	28
5083	TERMINAL SACRIFICE	5-SEP-03	28
5084	TERMINAL SACRIFICE	9-SEP-03	28

6-FEB-2004 10:21

Huntingdon Life Sciences 03-4254P

PAGE 308

APPENDIX V - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL ANIMAL TERMINATION HISTORY

FEMALES GROUP 1 0 MG/KG/DAY

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY
1575	TERMINAL SACRIFICE	4-SEP-03	28
1576	TERMINAL SACRIFICE	10-SEP-03	28
1577	TERMINAL SACRIFICE	4-SEP-03	28
1578	TERMINAL SACRIFICE	6-SEP-03	28
1579	TERMINAL SACRIFICE	4-SEP-03	28
1580	TERMINAL SACRIFICE	5-SEP-03	28
1581	TERMINAL SACRIFICE	4-SEP-03	28
1582	TERMINAL SACRIFICE	6-SEP-03	28
1583	TERMINAL SACRIFICE	7-SEP-03	28
1584	TERMINAL SACRIFICE	4-SEP-03	28
1585	TERMINAL SACRIFICE	6-SEP-03	28

6-FEB-2004 10:21

Huntingdon Life Sciences 03-4254P

PAGE 309

APPENDIX V - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL ANIMAL TERMINATION HISTORY

FEMALES GROUP 2 64 MG/KG/DAY

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY
2575	TERMINAL SACRIFICE	5-SEP-03	28
2576	TERMINAL SACRIFICE	9-SEP-03	28
2577	TERMINAL SACRIFICE	4-SEP-03	28
2578	TERMINAL SACRIFICE	3-SEP-03	28
2579	TERMINAL SACRIFICE	7-SEP-03	28
2580	TERMINAL SACRIFICE	7-SEP-03	28
2581	TERMINAL SACRIFICE	6-SEP-03	28
2582	TERMINAL SACRIFICE	3-SEP-03	28
2583	TERMINAL SACRIFICE	7-SEP-03	28
2584	TERMINAL SACRIFICE	5-SEP-03	28
2585	TERMINAL SACRIFICE	6-SEP-03	28

6-FEB-2004 10:21

Huntingdon Life Sciences 03-4254P

PAGE 310

APPENDIX V - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL ANIMAL TERMINATION HISTORY

FEMALES GROUP 3 160 MG/KG/DAY

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY
3575	TERMINAL SACRIFICE	5-SEP-03	28
3576	TERMINAL SACRIFICE	4-SEP-03	28
3577	TERMINAL SACRIFICE	12-SEP-03	28
3578	TERMINAL SACRIFICE	8-SEP-03	28
3579	TERMINAL SACRIFICE	4-SEP-03	28
3580	TERMINAL SACRIFICE	5-SEP-03	28
3581	TERMINAL SACRIFICE	6-SEP-03	28
3582	TERMINAL SACRIFICE	7-SEP-03	28
3583	TERMINAL SACRIFICE	7-SEP-03	28
3584	TERMINAL SACRIFICE	5-SEP-03	28
3585	TERMINAL SACRIFICE	8-SEP-03	28
3586	TERMINAL SACRIFICE	4-SEP-03	28

6-FEB-2004 10:21

Huntingdon Life Sciences 03-4254P

PAGE 311

APPENDIX V - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL ANIMAL TERMINATION HISTORY

FEMALES GROUP 4 400 MG/KG/DAY

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY
4575	TERMINAL SACRIFICE	5-SEP-03	28
4576	TERMINAL SACRIFICE	7-SEP-03	28
4577	TERMINAL SACRIFICE	6-SEP-03	28
4578	TERMINAL SACRIFICE	7-SEP-03	28
4579	TERMINAL SACRIFICE	7-SEP-03	28
4580	TERMINAL SACRIFICE	8-SEP-03	28
4581	TERMINAL SACRIFICE	5-SEP-03	28
4582	TERMINAL SACRIFICE	7-SEP-03	28
4583	TERMINAL SACRIFICE	7-SEP-03	28
4584	TERMINAL SACRIFICE	7-SEP-03	28
4585	TERMINAL SACRIFICE	6-SEP-03	28
4586	TERMINAL SACRIFICE	7-SEP-03	28

6-FEB-2004 10:21

Huntingdon Life Sciences 03-4254P

PAGE 312

APPENDIX V - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL ANIMAL TERMINATION HISTORY

FEMALES GROUP 5 1000 MG/KG/DAY

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY
5575	TERMINAL SACRIFICE	7-SEP-03	28
5576	TERMINAL SACRIFICE	5-SEP-03	28
5577	TERMINAL SACRIFICE	8-SEP-03	28
5578	TERMINAL SACRIFICE	9-SEP-03	28
5579	TERMINAL SACRIFICE	7-SEP-03	28
5580	TERMINAL SACRIFICE	6-SEP-03	28
5581	TERMINAL SACRIFICE	7-SEP-03	28
5582	TERMINAL SACRIFICE	4-SEP-03	28
5583	TERMINAL SACRIFICE	5-SEP-03	28
5584	TERMINAL SACRIFICE	7-SEP-03	28

6-FEB-2004 10:31

Huntingdon Life Sciences 03-4254P

PAGE 313

APPENDIX W - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL CLINICAL OBSERVATIONS

MALES GROUP 1 0 MG/KG/DAY

ANIMAL#	OBSERVATIONS	DAY OF	2
		STUDY	8
1075	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
1076	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
1077	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
1078	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
1079	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
1080	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
1081	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
1082	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
1083	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
1084	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

6-FEB-2004 10:31

Huntingdon Life Sciences 03-4254P

PAGE 314

APPENDIX W - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL CLINICAL OBSERVATIONS

MALES GROUP 1 0 MG/KG/DAY

ANIMAL#	OBSERVATIONS	DAY OF STUDY	2 8
1085	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

6-FEB-2004 10:31

Huntingdon Life Sciences 03-4254P

PAGE 315

APPENDIX W - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL CLINICAL OBSERVATIONS

MALES GROUP 2 64 MG/KG/DAY

ANIMAL#	OBSERVATIONS	DAY OF	2
		STUDY	8
2075	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
2076	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
2077	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
2078	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
2079	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
2080	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
2081	TERMINAL SACRIFICE		P
	ALOPECIA - EXTREMITIES/SNOUT		2
2082	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
2083	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
2084	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

6-FEB-2004 10:31

Huntingdon Life Sciences 03-4254P

PAGE 316

APPENDIX W - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL CLINICAL OBSERVATIONS

MALES GROUP 2 64 MG/KG/DAY

ANIMAL#	OBSERVATIONS	DAY OF STUDY	2 8
---------	--------------	-----------------	--------

2085	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

6-FEB-2004 10:31

Huntingdon Life Sciences 03-4254P

PAGE 317

APPENDIX W - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL CLINICAL OBSERVATIONS

MALES GROUP 3 160 MG/KG/DAY

ANIMAL#	OBSERVATIONS	DAY OF	2
		STUDY	8
3075	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
3076	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
3077	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
3078	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
3079	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
3080	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
3081	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
3082	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
3083	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
3084	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

6-FEB-2004 10:31

Huntingdon Life Sciences 03-4254P

PAGE 318

APPENDIX W - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL CLINICAL OBSERVATIONS

MALES GROUP 3 160 MG/KG/DAY

ANIMAL#	OBSERVATIONS	DAY OF STUDY	2 8
3085	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

6-FEB-2004 10:31

Huntingdon Life Sciences 03-4254P

PAGE 319

APPENDIX W - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL CLINICAL OBSERVATIONS

MALES GROUP 4 400 MG/KG/DAY

ANIMAL#	OBSERVATIONS	DAY OF	2
		STUDY	8
4075	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
4076	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
4077	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
4078	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
4079	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
4080	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
4081	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
4082	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
4083	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
4084	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

6-FEB-2004 10:31

Huntingdon Life Sciences 03-4254P

PAGE 320

APPENDIX W - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL CLINICAL OBSERVATIONS

MALES GROUP 4 400 MG/KG/DAY

ANIMAL#	OBSERVATIONS	DAY OF STUDY	2 8
4085	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
4086	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

6-FEB-2004 10:31

Huntingdon Life Sciences 03-4254P

PAGE 321

APPENDIX W - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL CLINICAL OBSERVATIONS

MALES GROUP 5 1000 MG/KG/DAY

ANIMAL#	OBSERVATIONS	DAY OF STUDY	2 8
5075	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P P
5076	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P P
5077	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P P
5078	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P P
5079	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P P
5080	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P P
5081	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P P
5082	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P P
5083	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P P
5084	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

6-FEB-2004 10:31

Huntingdon Life Sciences 03-4254P

PAGE 322

APPENDIX W - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP 1 0 MG/KG/DAY

ANIMAL#	OBSERVATIONS	DAY OF	2
		STUDY	8
1575	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P P
1576	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P P
1577	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P P
1578	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P P
1579	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P P
1580	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P P
1581	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P P
1582	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P P
1583	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P P
1584	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

6-FEB-2004 10:31

Huntingdon Life Sciences 03-4254P

PAGE 323

APPENDIX W - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP 1 0 MG/KG/DAY

ANIMAL#	OBSERVATIONS	DAY OF STUDY	2 8
---------	--------------	-----------------	--------

1585	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

6-FEB-2004 10:31

Huntingdon Life Sciences 03-4254P

PAGE 324

APPENDIX W - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP 2 64 MG/KG/DAY

ANIMAL#	OBSERVATIONS	DAY OF	2
		STUDY	8
2575	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P P
2576	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P P
2577	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P P
2578	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P P
2579	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P P
2580	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P P
2581	TERMINAL SACRIFICE ALOPECIA - EXTREMITIES/SNOUT		P 2
2582	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P P
2583	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P P
2584	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

6-FEB-2004 10:31

Huntingdon Life Sciences 03-4254P

PAGE 325

APPENDIX W - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP 2 64 MG/KG/DAY

ANIMAL#	OBSERVATIONS	DAY OF STUDY	2 8
2585	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

6-FEB-2004 10:31

Huntingdon Life Sciences 03-4254P

PAGE 326

APPENDIX W - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP 3 160 MG/KG/DAY

ANIMAL#	OBSERVATIONS	DAY OF	2
		STUDY	8
3575	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
3576	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
3577	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
3578	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
3579	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
3580	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
3581	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
3582	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
3583	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
3584	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

6-FEB-2004 10:31

Huntingdon Life Sciences 03-4254P

PAGE 327

APPENDIX W - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP 3 160 MG/KG/DAY

ANIMAL#	OBSERVATIONS	DAY OF	2
		STUDY	8
3585	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
3586	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

6-FEB-2004 10:31

Huntingdon Life Sciences 03-4254P

PAGE 328

APPENDIX W - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP 4 400 MG/KG/DAY

ANIMAL#	OBSERVATIONS	DAY OF STUDY	2 8
4575	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P P
4576	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P P
4577	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P P
4578	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P P
4579	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P P
4580	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P P
4581	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P P
4582	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P P
4583	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P P
4584	WITHIN NORMAL LIMITS TERMINAL SACRIFICE		P P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

6-FEB-2004 10:31

Huntingdon Life Sciences 03-4254P

PAGE 329

APPENDIX W - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP 4 400 MG/KG/DAY

ANIMAL#	OBSERVATIONS	DAY OF STUDY	2 8
4585	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
4586	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

6-FEB-2004 10:31

Huntingdon Life Sciences 03-4254P

PAGE 330

APPENDIX W - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP 5 1000 MG/KG/DAY

ANIMAL#	OBSERVATIONS	DAY OF	2
		STUDY	8
5575	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
5576	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
5577	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
5578	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
5579	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
5580	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
5581	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
5582	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
5583	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P
5584	WITHIN NORMAL LIMITS		P
	TERMINAL SACRIFICE		P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

6-FEB-2004 10:35

Huntingdon Life Sciences 03-4254P

PAGE331

APPENDIX X - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL BODY WEIGHTS (GRAMS)

MALES GROUP 1 0 MG/KG/DAY

ANIMAL#	DAY OF STUDY		
	21	24	28
1075	50	67	93
1076	54	70	95
1077	49	67	94
1078	57	74	105
1079	53	71	96
1080	58	76	106
1081	54	73	100
1082	55	73	99
1083	50	68	98
1084	54	72	100
1085	60	79	108
MEAN	54	72	99
S.D.	3.4	3.7	4.9
N	11	11	11

6-FEB-2004 10:35

Huntingdon Life Sciences 03-4254P

PAGE332

APPENDIX X - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL BODY WEIGHTS (GRAMS)

MALES GROUP 2 64 MG/KG/DAY

ANIMAL#	DAY OF STUDY		
	21	24	28
2075	51	70	96
2076	57	74	104
2077	59	79	107
2078	53	67	94
2079	50	68	91
2080	55	74	104
2081	60	80	107
2082	54	74	101
2083	64	82	109
2084	55	71	101
2085	52	71	99
MEAN	55	74	101
S.D.	4.5	4.9	5.7
N	11	11	11

6-FEB-2004 10:35

Huntingdon Life Sciences 03-4254P

PAGE333

APPENDIX X - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL BODY WEIGHTS (GRAMS)

MALES GROUP 3 160 MG/KG/DAY

ANIMAL#	DAY OF STUDY		
	21	24	28
3075	52	69	98
3076	55	72	102
3077	48	64	86
3078	44	60	87
3079	58	76	102
3080	52	69	95
3081	38	55	79
3082	66	86	119
3083	56	74	102
3084	57	75	102
3085	61	82	115
MEAN	53	71	99
S.D.	7.9	9.1	12.1
N	11	11	11

6-FEB-2004 10:35

Huntingdon Life Sciences 03-4254P

PAGE334

APPENDIX X - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL BODY WEIGHTS (GRAMS)

MALES GROUP 4 400 MG/KG/DAY

ANIMAL#	DAY OF STUDY		
	21	24	28
4075	49	67	93
4076	46	59	85
4077	45	58	86
4078	60	73	103
4079	50	64	93
4080	52	70	95
4081	52	67	97
4082	60	82	117
4083	63	77	110
4084	60	74	106
4085	63	77	105
4086	49	65	94
MEAN	54	69	99
S.D.	6.7	7.4	9.6
N	12	12	12

6-FEB-2004 10:35

Huntingdon Life Sciences 03-4254P

PAGE335

APPENDIX X - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL BODY WEIGHTS (GRAMS)

MALES GROUP 5 1000 MG/KG/DAY

ANIMAL#	DAY OF STUDY		
	21	24	28
5075	47	62	87
5076	42	61	83
5077	49	67	95
5078	46	62	89
5079	48	63	86
5080	53	70	98
5081	43	62	91
5082	42	44	66
5083	55	69	94
5084	43	58	85
MEAN	47	62	87
S.D.	4.6	7.4	9.1
N	10	10	10

6-FEB-2004 10:35

Huntingdon Life Sciences 03-4254P

PAGE336

APPENDIX X - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL BODY WEIGHTS (GRAMS)

FEMALES GROUP 1 0 MG/KG/DAY

ANIMAL#	DAY OF STUDY		
	21	24	28
1575	53	69	93
1576	48	62	86
1577	49	63	82
1578	57	73	95
1579	49	65	87
1580	55	71	96
1581	52	69	92
1582	50	65	88
1583	49	65	87
1584	55	68	92
1585	58	75	101
MEAN	52	68	91
S.D.	3.6	4.2	5.3
N	11	11	11

6-FEB-2004 10:35

Huntingdon Life Sciences 03-4254P

PAGE337

APPENDIX X - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL BODY WEIGHTS (GRAMS)

FEMALES GROUP 2 64 MG/KG/DAY

ANIMAL#	DAY OF STUDY		
	21	24	28
2575	50	63	84
2576	58	73	97
2577	53	68	92
2578	41	53	73
2579	47	61	80
2580	52	67	92
2581	51	65	89
2582	49	69	96
2583	67	85	113
2584	54	70	95
2585	55	72	95
MEAN	52	68	91
S.D.	6.5	8.0	10.3
N	11	11	11

6-FEB-2004 10:35

Huntingdon Life Sciences 03-4254P

PAGE338

APPENDIX X - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL BODY WEIGHTS (GRAMS)

FEMALES GROUP 3 160 MG/KG/DAY

ANIMAL#	DAY OF STUDY		
	21	24	28
3575	50	63	89
3576	47	62	83
3577	51	63	84
3578	41	52	77
3579	51	65	86
3580	52	69	94
3581	64	80	103
3582	41	58	82
3583	58	74	103
3584	56	72	95
3585	56	71	92
3586	33	44	62
MEAN	50	64	87
S.D.	8.6	9.8	11.5
N	12	12	12

6-FEB-2004 10:35

Huntingdon Life Sciences 03-4254P

PAGE339

APPENDIX X - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL BODY WEIGHTS (GRAMS)

FEMALES GROUP 4 400 MG/KG/DAY

ANIMAL#	DAY OF STUDY		
	21	24	28
4575	55	66	90
4576	43	54	74
4577	45	57	77
4578	63	76	103
4579	42	59	84
4580	50	67	87
4581	51	61	83
4582	55	70	99
4583	55	69	95
4584	59	70	92
4585	64	77	100
4586	50	61	87
MEAN	53	66	89
S.D.	7.2	7.3	9.3
N	12	12	12

6-FEB-2004 10:35

Huntingdon Life Sciences 03-4254P

PAGE340

APPENDIX X - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL BODY WEIGHTS (GRAMS)

FEMALES GROUP 5 1000 MG/KG/DAY

ANIMAL#	DAY OF STUDY		
	21	24	28
5575	55	66	85
5576	46	59	82
5577	39	52	74
5578	42	51	76
5579	48	63	87
5580	45	62	84
5581	52	67	88
5582	46	62	83
5583	62	76	97
5584	57	67	86
MEAN	49	62	84
S.D.	7.3	7.2	6.5
N	10	10	10

6-FEB-2004 10:38

Huntingdon Life Sciences 03-4254P

PAGE341

APPENDIX Y - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL BODY WEIGHT GAIN (GRAMS)

MALES GROUP 1 0 MG/KG/DAY

ANIMAL#	DAY OF STUDY		
	21-24	24-28	21-28
1075	16	26	43
1076	16	25	41
1077	18	27	45
1078	17	30	47
1079	18	26	43
1080	18	30	48
1081	19	27	46
1082	18	27	44
1083	18	30	48
1084	18	28	46
1085	19	29	48
MEAN	18	28	45
S.D.	1.0	1.9	2.5
N	11	11	11

6-FEB-2004 10:38

Huntingdon Life Sciences 03-4254P

PAGE342

APPENDIX Y - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL BODY WEIGHT GAIN (GRAMS)

MALES GROUP 2 64 MG/KG/DAY

ANIMAL#	DAY OF STUDY		
	21-24	24-28	21-28
2075	20	26	46
2076	18	30	48
2077	20	28	48
2078	15	26	41
2079	18	24	42
2080	19	30	49
2081	19	27	46
2082	20	27	47
2083	17	27	45
2084	16	30	46
2085	20	27	47
MEAN	18	28	46
S.D.	1.8	1.9	2.5
N	11	11	11

6-FEB-2004 10:38

Huntingdon Life Sciences 03-4254P

PAGE343

APPENDIX Y - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL BODY WEIGHT GAIN (GRAMS)

MALES GROUP 3 160 MG/KG/DAY

ANIMAL#	DAY OF STUDY		
	21-24	24-28	21-28
3075	17	29	46
3076	17	30	47
3077	16	21	37
3078	16	27	43
3079	17	26	43
3080	16	26	43
3081	17	24	41
3082	20	34	54
3083	17	28	45
3084	18	27	45
3085	21	33	54
MEAN	18	28	45
S.D.	1.7	3.6	5.1
N	11	11	11

6-FEB-2004 10:38

Huntingdon Life Sciences 03-4254P

PAGE344

APPENDIX Y - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL BODY WEIGHT GAIN (GRAMS)

MALES GROUP 4 400 MG/KG/DAY

ANIMAL#	DAY OF STUDY		
	21-24	24-28	21-28
4075	18	26	44
4076	14	26	39
4077	13	29	41
4078	13	31	43
4079	14	29	43
4080	18	25	43
4081	15	31	46
4082	22	35	57
4083	14	33	47
4084	14	32	46
4085	14	28	42
4086	15	29	45
MEAN	15	29	45
S.D.	2.7	3.1	4.4
N	12	12	12

6-FEB-2004 10:38

Huntingdon Life Sciences 03-4254P

PAGE345

APPENDIX Y - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL BODY WEIGHT GAIN (GRAMS)

MALES GROUP 5 1000 MG/KG/DAY

ANIMAL#	DAY OF STUDY		
	21-24	24-28	21-28
5075	15	25	40
5076	19	23	41
5077	18	28	46
5078	16	27	43
5079	16	23	38
5080	17	28	45
5081	19	28	47
5082	1	22	23
5083	13	26	39
5084	15	27	41
MEAN	15	26	40
S.D.	5.1	2.5	6.8
N	10	10	10

6-FEB-2004 10:38

Huntingdon Life Sciences 03-4254P

PAGE346

APPENDIX Y - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL BODY WEIGHT GAIN (GRAMS)

FEMALES GROUP 1 0 MG/KG/DAY

ANIMAL#	DAY OF STUDY		
	21-24	24-28	21-28
1575	16	24	39
1576	14	24	39
1577	14	20	33
1578	15	22	38
1579	16	22	38
1580	16	25	41
1581	17	23	40
1582	15	23	38
1583	16	23	39
1584	14	23	37
1585	17	26	43
MEAN	15	23	39
S.D.	1.2	1.6	2.5
N	11	11	11

6-FEB-2004 10:38

Huntingdon Life Sciences 03-4254P

PAGE347

APPENDIX Y - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL BODY WEIGHT GAIN (GRAMS)

FEMALES GROUP 2 64 MG/KG/DAY

ANIMAL#	DAY OF STUDY		
	21-24	24-28	21-28
2575	13	20	34
2576	15	24	39
2577	16	23	39
2578	12	20	32
2579	14	19	33
2580	15	25	40
2581	14	23	38
2582	21	27	47
2583	18	28	46
2584	16	26	42
2585	17	24	40
MEAN	16	24	39
S.D.	2.4	2.7	4.9
N	11	11	11

6-FEB-2004 10:38

Huntingdon Life Sciences 03-4254P

PAGE348

APPENDIX Y - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL BODY WEIGHT GAIN (GRAMS)

FEMALES GROUP 3 160 MG/KG/DAY

ANIMAL#	DAY OF STUDY		
	21-24	24-28	21-28
3575	13	26	39
3576	15	21	36
3577	12	21	33
3578	11	25	36
3579	14	21	35
3580	17	26	42
3581	15	23	39
3582	17	24	41
3583	16	29	45
3584	16	23	39
3585	14	21	36
3586	11	17	29
MEAN	14	23	37
S.D.	2.0	3.1	4.4
N	12	12	12

6-FEB-2004 10:38

Huntingdon Life Sciences 03-4254P

PAGE349

APPENDIX Y - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL BODY WEIGHT GAIN (GRAMS)

FEMALES GROUP 4 400 MG/KG/DAY

ANIMAL#	DAY OF STUDY		
	21-24	24-28	21-28
4575	11	24	35
4576	12	20	32
4577	12	20	32
4578	14	27	41
4579	16	25	41
4580	17	20	37
4581	10	22	32
4582	15	29	44
4583	14	26	40
4584	11	22	33
4585	13	24	36
4586	11	26	37
MEAN	13	24	37
S.D.	2.2	3.0	4.1
N	12	12	12

6-FEB-2004 10:38

Huntingdon Life Sciences 03-4254P

PAGE350

APPENDIX Y - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL BODY WEIGHT GAIN (GRAMS)

FEMALES GROUP 5 1000 MG/KG/DAY

ANIMAL#	DAY OF STUDY		
	21-24	24-28	21-28
5575	10	19	29
5576	13	23	36
5577	13	22	35
5578	10	24	34
5579	15	24	40
5580	18	22	40
5581	14	21	36
5582	15	22	37
5583	13	21	34
5584	10	19	29
MEAN	13	22	35
S.D.	2.6	1.8	3.7
N	10	10	10

	Individual Feed Consumption Values F1 Treated Animals Preface	Appendix Z
--	---	------------

Note:

Both male and female animals were double housed at the time feed consumption was recorded. One set of animals in Group 5 was triple housed because of one extra animal in the group. Feed consumption values represent the combined amount of feed consumed per cage per study day interval.

Definitions:

IW=Invalid Weight (feed values could not be determined due to a contaminated feeder occurring in the midpoint of the 21-28 day interval that was replaced with a fresh feeder on Day 24)

CF=Contaminated Feeder

Pup # 5 and 14 (in Groups 3 and 5, respectively) are described under the dam number (in addition to the pup number) because the pup was not re-assigned its own "on-study" number.

APPENDIX Z - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENT TOXICITY SCREENING IN RATS

INDIVIDUAL FEED CONSUMPTION VALUES (GRAMS/DAY)

GROUP 1 0 MG/KG/DAY

ANIMAL #'S	DAYS OF STUDY (GRAMS/CAGE/DAY)		
	21- 24	24-28	21-28
1075/1575	18	26	44
1076/1576	21	30	51
1077/1577	15	23	38
1078/1578	CF	29	IW
1079/1579	20	25	45
1080/1580	21	27	48
1081/1581	18	26	44
1082/1582	19	25	44
1083/1583	17	25	42
1084/1584	18	CF	CF
1085/1585	20	29	49
MEAN/ANIMAL/DAY	9.4	13.2	22.5
S.D.	0.9	1.1	1.9
N	10	10	9

CF=Contaminated Feeder; IW=Invalid Weight

APPENDIX Z - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENT TOXICITY SCREENING IN RATS

INDIVIDUAL FEED CONSUMPTION VALUES (GRAMS/DAY)

GROUP 2 64 MG/KG/DAY

ANIMAL #'S	DAYS OF STUDY (GRAMS/CAGE/DAY)		
	21- 24	24-28	21-28
2075/2575	17	26	43
2076/2576	18	29	47
2077/2577	19	28	46
2078/2578 ^a	11	24	35
2079/2579	21	24	44
2080/2580	22	30	51
2081/2581	21	29	49
2082/2582 ^a	14	28	41
2083/2583	25	30	55
2084/2584	20	29	49
2085/2585	CF	29	IW
MEAN/ANIMAL/DAY	9.3	13.8	23.0
S.D.	1.9	1.1	2.8
N	10	11	10

CF=Contaminated Feeder; IW=Invalid Weight; a=food consumption for these animals i

APPENDIX Z - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENT TOXICITY SCREENING IN RATS

INDIVIDUAL FEED CONSUMPTION VALUES (GRAMS/DAY)

GROUP 3 160 MG/KG/DAY

ANIMAL #'S	DAYS OF STUDY (GRAMS/CAGE/DAY)		
	21- 24	24-28	21-28
3075/3575	19	CF	CF
3076/3576	CF	26	IW
3077/3577	CF	CF	IW
3078/3578	16	CF	CF
3079/3579	20	26	46
3080/3580	18	25	43
3081/3582	17	23	40
3082/3583	22	32	54
3083/3584	19	CF	CF
3084/3585	19	30	49
3086/3586	17	24	41
3581/3469 (Pup # 5)	21	28	49
MEAN/ANIMAL/DAY	9.4	13.4	23.0
S.D.	0.9	1.4	2.4
N	10	8	7

CF=Contaminated Feeder, IW=Invalid Weight

APPENDIX Z - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENT TOXICITY SCREENING IN RATS

INDIVIDUAL FEED CONSUMPTION VALUES (GRAMS/DAY)

GROUP 4 400 MG/KG/DAY

ANIMAL #'S	DAYS OF STUDY (GRAMS/CAGE/DAY)		
	21- 24	24-28	21-28
4075/4575	16	29	45
4076/4576	18	26	44
4077/4577	15	CF	CF
4078/4578	22	28	48
4079/4579	17	CF	CF
4080/4580	21	26	47
4081/4581	16	27	43
4082/4582	21	32	53
4083/4583	21	28	49
4084/4584	21	28	49
4085/4585	20	31	51
4086/4586	19	25	44
MEAN/ANIMAL/DAY	9.5	14.0	23.8
S.D.	1.2	1.0	1.7
N	12	10	10

CF=Contaminated Feeder

APPENDIX Z - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENT TOXICITY SCREENING IN RATS

INDIVIDUAL FEED CONSUMPTION VALUES (GRAMS/DAY)

GROUP 5 1000 MG/KG/DAY

ANIMAL #'S	DAYS OF STUDY (GRAMS/CAGE/DAY)		
	21- 24	24-28	21-28
5075/5576	15	CF	CF
5076/5577	CF	24	IW
5077,5084/5578	CF	42	IW
5078/5579	CF	26	IW
5079/5580	CF	25	IW
5080/5581	20	27	47
5081/5582	CF	24	IW
5082/5573 (Pup # 14)	8	CF	CF
5083/5583	19	27	46
5575/5584	17	23	40
MEAN/ANIMAL/DAY	7.9	12.8	22.2
S.D.	2.5	0.9	2.0
N	5	8	3

CF=Contaminated Feeder, IW=Invalid Weight

Huntingdon Life Sciences 03-4254

APPENDIX AA - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

ORGAN AND FINAL BODY WEIGHTS

MALES GROUP 1 0 MG/KG/DAY

Animal Number	FINAL BODY WEIGHT g	TESTIS - RIGHT		TESTIS - LEFT		EPIDIDYMIS LEFT		EPIDIDYMIS RIGHT		KIDNEY LEFT		KIDNEY RIGHT	
		Weight g	Ratio	Weight g	Ratio	Weight g	Ratio	Weight g	Ratio	Weight g	Ratio	Weight g	Ratio
1063	480	1.6890	0.0035	1.6869	0.0035	0.6355	0.0013	0.6466	0.0013	1.8301	0.0038	1.8869	0.0039
1064	557	1.4591	0.0026	1.5544	0.0028	0.6679	0.0012	0.7318	0.0013	2.0742	0.0037	1.9470	0.0035
1065	485	1.6463	0.0034	1.6444	0.0034	0.7270	0.0015	0.7137	0.0015	1.5793	0.0033	1.5760	0.0033
1066	518	1.7627	0.0034	1.8232	0.0035	0.7138	0.0014	0.6360	0.0012	1.8069	0.0035	1.8702	0.0036
1067	602	1.9639	0.0033	1.9530	0.0032	0.7424	0.0012	0.7251	0.0012	1.8801	0.0031	2.0953	0.0035
1068	541	1.8049	0.0033	1.7187	0.0032	0.6902	0.0013	0.7128	0.0013	2.1240	0.0039	1.9979	0.0037
1069	569	1.5795	0.0028	1.5586	0.0027	0.6317	0.0011	0.6341	0.0011	2.0542	0.0036	2.1696	0.0038
1070	468	1.5426	0.0033	1.5085	0.0032	0.5963	0.0013	0.6362	0.0014	1.7414	0.0037	1.8156	0.0039
1071	575	1.6497	0.0029	1.6448	0.0029	0.6731	0.0012	0.6779	0.0012	1.9451	0.0034	1.8976	0.0033
1072	581	1.8536	0.0032	1.8583	0.0032	0.7556	0.0013	0.7721	0.0013	2.1165	0.0036	2.1717	0.0037
1073	623	1.6686	0.0027	1.6900	0.0027	0.6417	0.0010	0.6612	0.0011	2.3368	0.0037	2.2043	0.0035
1074	514	1.8814	0.0037	1.7746	0.0035	0.7001	0.0014	0.7988	0.0016	2.0208	0.0039	2.0622	0.0040

RATIO = ORGAN WEIGHT/BODY WEIGHT

Huntingdon Life Sciences 03-4254

APPENDIX AA - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

ORGAN AND FINAL BODY WEIGHTS

MALES GROUP 2 64 MG/KG/DAY

Animal Number	FINAL BODY WEIGHT g	TESTIS - RIGHT		TESTIS - LEFT		EPIDIDYMIS LEFT		EPIDIDYMIS RIGHT		KIDNEY LEFT		KIDNEY RIGHT	
		Weight g	Ratio	Weight g	Ratio	Weight g	Ratio	Weight g	Ratio	Weight g	Ratio	Weight g	Ratio
2063	550	1.8272	0.0033	1.8491	0.0034	0.7752	0.0014	1.5485	0.0028	2.1225	0.0039	2.1739	0.0040
2064	498	1.7616	0.0035	1.6790	0.0034	0.6503	0.0013	0.6310	0.0013	1.8597	0.0037	2.0672	0.0041
2065	561	1.4391	0.0026	1.4203	0.0025	0.6143	0.0011	0.6191	0.0011	2.0077	0.0036	1.9481	0.0035
2066	492	1.8948	0.0039	1.9070	0.0039	0.7276	0.0015	0.7167	0.0015	1.8903	0.0038	1.9719	0.0040
2067	551	1.7976	0.0033	1.7698	0.0032	0.6990	0.0013	0.7251	0.0013	2.2589	0.0041	2.1620	0.0039
2068	539	1.9211	0.0036	2.0112	0.0037	0.7467	0.0014	0.7374	0.0014	2.3083	0.0043	2.1636	0.0040
2069	485	1.5495	0.0032	1.5280	0.0032	0.5900	0.0012	0.6746	0.0014	2.0833	0.0043	1.8851	0.0039
2070	554	1.7395	0.0031	1.7070	0.0031	0.7036	0.0013	0.7364	0.0013	2.1654	0.0039	2.1966	0.0040
2071	526	1.7522	0.0033	1.7475	0.0033	0.7277	0.0014	0.7269	0.0014	1.7527	0.0033	1.7879	0.0034
2072	543	1.8578	0.0034	1.8107	0.0033	0.6850	0.0013	0.6817	0.0013	2.2746	0.0042	2.4452	0.0045
2073	603	1.9900	0.0033	2.0340	0.0034	0.7301	0.0012	0.7574	0.0013	2.0941	0.0035	2.1773	0.0036
2074	536	1.8041	0.0034	1.7405	0.0032	0.7236	0.0013	0.7146	0.0013	2.1499	0.0040	2.1198	0.0040

RATIO = ORGAN WEIGHT/BODY WEIGHT

Huntingdon Life Sciences 03-4254

APPENDIX AA - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

ORGAN AND FINAL BODY WEIGHTS

MALES GROUP 3 160 MG/KG/DAY

Animal Number	FINAL BODY WEIGHT g	TESTIS - RIGHT		TESTIS - LEFT		EPIDIDYMIS LEFT		EPIDIDYMIS RIGHT		KIDNEY LEFT		KIDNEY RIGHT	
		Weight g	Ratio	Weight g	Ratio	Weight g	Ratio	Weight g	Ratio	Weight g	Ratio	Weight g	Ratio
3063	554	1.7387	0.0031	1.7027	0.0031	0.6990	0.0013	0.7340	0.0013	2.0068	0.0036	2.0625	0.0037
3064	514	1.6413	0.0032	1.6824	0.0033	0.6786	0.0013	0.6544	0.0013	2.0558	0.0040	1.9898	0.0039
3065	585	1.7585	0.0030	1.7543	0.0030	0.7209	0.0012	0.7071	0.0012	2.1547	0.0037	2.3825	0.0041
3066	493	1.8192	0.0037	1.8366	0.0037	0.6998	0.0014	0.7443	0.0015	2.0100	0.0041	2.0186	0.0041
3067	533	1.5925	0.0030	1.6385	0.0031	0.7425	0.0014	0.7013	0.0013	2.1307	0.0040	2.1581	0.0040
3068	469	1.9855	0.0042	1.9132	0.0041	0.6696	0.0014	0.7159	0.0015	1.8726	0.0040	1.9361	0.0041
3069	465	1.8761	0.0040	1.8465	0.0040	0.7126	0.0015	0.7643	0.0016	1.9136	0.0041	1.9171	0.0041
3070	518	1.8750	0.0036	1.8410	0.0036	0.7355	0.0014	0.6945	0.0013	2.7577	0.0053	2.0926	0.0040
3071	485	1.6104	0.0033	1.5636	0.0032	0.6274	0.0013	0.6674	0.0014	2.7532	0.0057	2.0160	0.0042
3072	534	1.9236	0.0036	1.9364	0.0036	0.7387	0.0014	0.8103	0.0015	1.7956	0.0034	1.9493	0.0037
3073	552	1.8907	0.0034	1.9977	0.0036	0.6899	0.0013	0.6564	0.0012	1.9949	0.0036	2.1635	0.0039
3074	559	1.6978	0.0030	1.6879	0.0030	0.6862	0.0012	0.7214	0.0013	2.2856	0.0041	2.3372	0.0042

RATIO = ORGAN WEIGHT/BODY WEIGHT

Huntingdon Life Sciences 03-4254

APPENDIX AA - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

ORGAN AND FINAL BODY WEIGHTS

MALES GROUP 4 400 MG/KG/DAY

Animal Number	FINAL BODY WEIGHT g	TESTIS - RIGHT		TESTIS - LEFT		EPIDIDYMIS LEFT		EPIDIDYMIS RIGHT		KIDNEY LEFT		KIDNEY RIGHT	
		Weight g	Ratio	Weight g	Ratio	Weight g	Ratio	Weight g	Ratio	Weight g	Ratio	Weight g	Ratio
4063	537	1.6873	0.0031	1.6604	0.0031	0.7226	0.0013	0.7257	0.0014	2.2570	0.0042	2.3350	0.0043
4064	486	1.7662	0.0036	1.7836	0.0037	0.6708	0.0014	0.6529	0.0013	2.1756	0.0045	2.0156	0.0042
4065	460	1.8573	0.0040	1.7989	0.0039	0.7195	0.0016	0.7151	0.0016	1.8076	0.0039	2.2115	0.0048
4066	553	1.7249	0.0031	1.7582	0.0032	0.7696	0.0014	0.7422	0.0013	2.3010	0.0042	2.3577	0.0043
4067	564	1.6772	0.0030	1.6620	0.0029	0.6344	0.0011	0.6573	0.0012	2.0917	0.0037	2.1896	0.0039
4068	558	1.8291	0.0033	1.8316	0.0033	0.6809	0.0012	0.7069	0.0013	2.3899	0.0043	2.3452	0.0042
4069	527	1.8390	0.0035	1.7889	0.0034	0.7025	0.0013	0.7678	0.0015	2.2556	0.0043	2.3063	0.0044
4070	553	1.8645	0.0034	1.8454	0.0033	0.6746	0.0012	0.7018	0.0013	2.4282	0.0044	2.4277	0.0044
4071	594	2.0493	0.0035	2.0172	0.0034	0.7258	0.0012	0.6923	0.0012	2.1789	0.0037	2.1576	0.0036
4072	519	1.6726	0.0032	1.6757	0.0032	0.6728	0.0013	0.6725	0.0013	2.3067	0.0044	2.4151	0.0047
4073	541	1.8441	0.0034	1.8781	0.0035	0.7273	0.0013	0.6973	0.0013	2.1453	0.0040	2.1630	0.0040
4074	544	1.8671	0.0034	1.9440	0.0036	0.7568	0.0014	0.7116	0.0013	2.0853	0.0038	2.1929	0.0040

RATIO = ORGAN WEIGHT/BODY WEIGHT

Huntingdon Life Sciences 03-4254

APPENDIX AA - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

ORGAN AND FINAL BODY WEIGHTS

MALES GROUP 5 1000 MG/KG/DAY

Animal Number	FINAL BODY WEIGHT g	TESTIS - RIGHT		TESTIS - LEFT		EPIDIDYMIS LEFT		EPIDIDYMIS RIGHT		KIDNEY LEFT		KIDNEY RIGHT	
		Weight g	Ratio	Weight g	Ratio	Weight g	Ratio	Weight g	Ratio	Weight g	Ratio	Weight g	Ratio
5063	493	1.8542	0.0038	1.9405	0.0039	0.6612	0.0013	0.6446	0.0013	2.2950	0.0047	2.2644	0.0046
5064	571	1.7065	0.0030	1.7707	0.0031	0.6535	0.0011	0.6117	0.0011	2.5000	0.0044	2.4774	0.0043
5065	544	1.9417	0.0036	1.9672	0.0036	0.7141	0.0013	0.7241	0.0013	2.5150	0.0046	2.4742	0.0045
5066	471	1.8913	0.0040	1.8948	0.0040	0.6836	0.0015	0.6900	0.0015	2.0946	0.0044	2.1373	0.0045
5067	502	1.7690	0.0035	1.7829	0.0035	0.6521	0.0013	0.6570	0.0013	2.5048	0.0050	2.5364	0.0050
5068	529	1.8648	0.0035	1.9067	0.0036	0.7504	0.0014	0.7396	0.0014	2.2319	0.0042	2.3838	0.0045
5069	453	1.8277	0.0040	1.8857	0.0042	0.6649	0.0015	0.6747	0.0015	2.1227	0.0047	2.2927	0.0051
5070	573	1.8365	0.0032	1.8488	0.0032	0.6753	0.0012	0.6947	0.0012	2.3098	0.0040	2.4175	0.0042
5071	466	1.9525	0.0042	1.9098	0.0041	0.7176	0.0015	0.6867	0.0015	2.3958	0.0051	2.3774	0.0051
5072	509	1.8598	0.0037	1.8873	0.0037	0.6638	0.0013	0.6213	0.0012	2.4912	0.0049	2.4536	0.0048
5073	486	1.5927	0.0033	1.5093	0.0031	0.6172	0.0013	0.6675	0.0014	2.1759	0.0045	2.2715	0.0047
5074	483	1.8428	0.0038	1.7788	0.0037	0.5916	0.0012	0.5889	0.0012	2.0449	0.0042	2.3420	0.0048

RATIO = ORGAN WEIGHT/BODY WEIGHT

Huntingdon Life Sciences 03-4254

APPENDIX AA - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

ORGAN AND FINAL BODY WEIGHTS

MALES GROUP 1 0 MG/KG/DAY

LIVER			
Animal	FINAL BODY		
Number	WEIGHT	Weight	Ratio
	g	g	
<hr/>			
1063	480	17.3467	0.0361
1064	557	21.5973	0.0388
1065	485	18.4735	0.0381
1066	518	17.5394	0.0339
1067	602	21.9091	0.0364
1068	541	21.4027	0.0395
1069	569	23.9426	0.0421
1070	468	18.0717	0.0386
1071	575	21.6865	0.0377
1072	581	25.1470	0.0433
1073	623	26.8122	0.0430
1074	514	18.4697	0.0359

RATIO = ORGAN WEIGHT/BODY WEIGHT

Huntingdon Life Sciences 03-4254

APPENDIX AA - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

ORGAN AND FINAL BODY WEIGHTS

MALES GROUP 2 64 MG/KG/DAY

LIVER			
Animal	FINAL BODY	-----	
Number	WEIGHT	Weight	Ratio
	g	g	

2063	550	21.8579	0.0398
2064	498	19.9471	0.0400
2065	561	20.3224	0.0362
2066	492	19.3077	0.0393
2067	551	23.5207	0.0427
2068	539	21.8205	0.0405
2069	485	16.3962	0.0338
2070	554	21.6512	0.0391
2071	526	19.2282	0.0365
2072	543	21.3172	0.0393
2073	603	23.1894	0.0384
2074	536	20.7592	0.0387

RATIO = ORGAN WEIGHT/BODY WEIGHT

Huntingdon Life Sciences 03-4254

APPENDIX AA - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

ORGAN AND FINAL BODY WEIGHTS

MALES GROUP 3 160 MG/KG/DAY

LIVER			
Animal	FINAL BODY	-----	
Number	WEIGHT	Weight	Ratio
	g	g	

3063	554	23.1367	0.0418
3064	514	18.9407	0.0368
3065	585	24.3919	0.0417
3066	493	20.1661	0.0409
3067	533	20.5392	0.0385
3068	469	17.9750	0.0383
3069	465	17.9394	0.0386
3070	518	21.3229	0.0412
3071	485	19.0514	0.0392
3072	534	17.9868	0.0337
3073	552	19.8851	0.0360
3074	559	22.2318	0.0397

RATIO = ORGAN WEIGHT/BODY WEIGHT

Huntingdon Life Sciences 03-4254

APPENDIX AA - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

ORGAN AND FINAL BODY WEIGHTS

MALES GROUP 4 400 MG/KG/DAY

LIVER			
Animal	FINAL BODY	-----	
Number	WEIGHT	Weight	Ratio
	g	g	

4063	537	20.8671	0.0388
4064	486	20.6305	0.0425
4065	460	18.3508	0.0399
4066	553	20.4587	0.0370
4067	564	21.0267	0.0373
4068	558	18.7695	0.0336
4069	527	20.6123	0.0391
4070	553	22.7048	0.0411
4071	594	23.9864	0.0404
4072	519	19.9691	0.0385
4073	541	19.7019	0.0364
4074	544	19.0160	0.0349

RATIO = ORGAN WEIGHT/BODY WEIGHT			

18-DEC-2003 12:32

PAGE 366

Huntingdon Life Sciences 03-4254

APPENDIX AA - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

ORGAN AND FINAL BODY WEIGHTS

MALES GROUP 5 1000 MG/KG/DAY

LIVER

Animal Number	FINAL BODY WEIGHT g	Weight g	Ratio
5063	493	24.0157	0.0487
5064	571	27.6452	0.0484
5065	544	24.9891	0.0459
5066	471	24.3025	0.0516
5067	502	21.9264	0.0437
5068	529	21.1361	0.0399
5069	453	20.9210	0.0462
5070	573	23.2553	0.0406
5071	466	21.1484	0.0454
5072	509	21.5986	0.0425
5073	486	21.0801	0.0434
5074	483	19.9189	0.0412

RATIO = ORGAN WEIGHT/BODY WEIGHT

Huntingdon Life Sciences 03-4254

APPENDIX AA - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

ORGAN AND FINAL BODY WEIGHTS

FEMALES GROUP 1 0 MG/KG/DAY

Animal Number	FINAL BODY WEIGHT g	KIDNEY LEFT		KIDNEY RIGHT		LIVER	
		Weight g	Ratio	Weight g	Ratio	Weight g	Ratio
1563	364	1.5767	0.0043	1.4156	0.0039	20.7393	0.0570
1564	337	1.3356	0.0040	1.4505	0.0043	17.4985	0.0520
1565	335	1.5654	0.0047	1.5190	0.0045	20.1456	0.0601
1566	334	1.3716	0.0041	1.4051	0.0042	16.9415	0.0508
1567 ^a NP						10.6682	
1568	291	1.2423	0.0043	1.3333	0.0046	16.8283	0.0577
1569	327	1.3838	0.0042	1.4416	0.0044	19.3079	0.0591
1570	353	1.4422	0.0041	1.2600	0.0036	21.6525	0.0613
1571	327	1.5681	0.0048	1.5667	0.0048	15.7260	0.0481
1572	322	1.4481	0.0045	1.5194	0.0047	17.7693	0.0551
1573	326	1.2224	0.0038	1.1899	0.0037	16.3473	0.0502
1574	335	1.4742	0.0044	1.4048	0.0042	16.2009	0.0484

RATIO = ORGAN WEIGHT/BODY WEIGHT

NP=NOT PREGNANT

x=EXCLUDED FROM MEAN

^aKidney weights were taken together instead of separately.

Huntingdon Life Sciences 03-4254

APPENDIX AA - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

ORGAN AND FINAL BODY WEIGHTS

FEMALES GROUP 2 64 MG/KG/DAY

Animal Number	FINAL BODY WEIGHT g	KIDNEY LEFT		KIDNEY RIGHT		LIVER	
		Weight g	Ratio	Weight g	Ratio	Weight g	Ratio
2563	351	1.5825	0.0045	1.5212	0.0043	20.2410	0.0577
2564	378	1.4009	0.0037	1.5323	0.0041	20.2007	0.0535
2565	310	1.3999	0.0045	1.3847	0.0045	16.0709	0.0518
2566	274	1.1927	0.0043	1.2083	0.0044	14.2219	0.0518
2567	319	1.2989	0.0041	1.2740	0.0040	16.4411	0.0516
2568	332	1.4024	0.0042	1.4631	0.0044	18.3916	0.0554
2569	310	1.3384	0.0043	1.3842	0.0045	15.8873	0.0513
2570	366	1.4950	0.0041	1.6119	0.0044	17.5920	0.0481
2571	360	1.4629	0.0041	1.4822	0.0041	17.5348	0.0487
2572x ^a NP						10.7672	
2573	354	1.5986	0.0045	1.5978	0.0045	19.1031	0.0540
2574	315	1.2374	0.0039	1.3752	0.0044	15.6103	0.0496

RATIO = ORGAN WEIGHT/BODY WEIGHT

NP=NOT PREGNANT

x=EXCLUDED FROM MEAN

^a Kidney weights were taken together instead of separately.

Huntingdon Life Sciences 03-4254

APPENDIX AA - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

ORGAN AND FINAL BODY WEIGHTS

FEMALES GROUP 3 160 MG/KG/DAY

Animal Number	FINAL BODY WEIGHT g	KIDNEY LEFT		KIDNEY RIGHT		LIVER	
		Weight g	Ratio	Weight g	Ratio	Weight g	Ratio
3563	334	1.7026	0.0051	1.6960	0.0051	17.6365	0.0527
3564	355	1.5572	0.0044	1.4772	0.0042	18.7766	0.0528
3565	353	1.3480	0.0038	1.2819	0.0036	18.4285	0.0523
3566	336	1.5066	0.0045	1.6096	0.0048	13.6686	0.0407
3567	289	1.3730	0.0048	1.3883	0.0048	14.9209	0.0516
3568	324	1.3174	0.0041	1.3780	0.0043	17.9937	0.0555
3569	298	1.2453	0.0042	1.2085	0.0041	12.9327	0.0434
3570	275	1.0881	0.0040	1.0529	0.0038	13.0082	0.0474
3571	344	1.4642	0.0043	1.4579	0.0042	17.7494	0.0517
3572	315	1.3589	0.0043	1.3755	0.0044	19.0156	0.0604
3573	349	1.5734	0.0045	1.6282	0.0047	19.9013	0.0570
3574	347	1.4671	0.0042	1.4663	0.0042	18.4588	0.0533

RATIO = ORGAN WEIGHT/BODY WEIGHT

Huntingdon Life Sciences 03-4254

APPENDIX AA - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

ORGAN AND FINAL BODY WEIGHTS

FEMALES GROUP 4 400 MG/KG/DAY

Animal Number	FINAL BODY WEIGHT g	KIDNEY LEFT		KIDNEY RIGHT		LIVER	
		Weight g	Ratio	Weight g	Ratio	Weight g	Ratio
4563	331	1.3324	0.0040	1.3205	0.0040	20.1724	0.0609
4564	295	1.4342	0.0049	1.4845	0.0050	16.5302	0.0561
4565	335	1.5681	0.0047	1.5101	0.0045	17.4537	0.0521
4566	312	1.3595	0.0044	1.3379	0.0043	17.1753	0.0550
4567	333	1.3621	0.0041	1.3985	0.0042	20.1951	0.0606
4568	364	1.6785	0.0046	1.6838	0.0046	19.4891	0.0536
4569	361	1.6776	0.0046	1.6480	0.0046	20.9698	0.0580
4570	354	1.5727	0.0044	1.5850	0.0045	20.2601	0.0573
4571	286	1.1067	0.0039	1.1645	0.0041	13.0864	0.0458
4572	344	1.4927	0.0043	1.5364	0.0045	19.5559	0.0568
4573	346	1.5277	0.0044	1.4680	0.0042	17.5509	0.0507
4574	351	1.3746	0.0039	1.4235	0.0041	18.3671	0.0524

RATIO = ORGAN WEIGHT/BODY WEIGHT

Huntingdon Life Sciences 03-4254

APPENDIX AA - F0 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

ORGAN AND FINAL BODY WEIGHTS

FEMALES GROUP 5 1000 MG/KG/DAY

Animal Number	FINAL BODY WEIGHT g	KIDNEY LEFT		KIDNEY RIGHT		LIVER	
		Weight g	Ratio	Weight g	Ratio	Weight g	Ratio
5563	331	1.4699	0.0044	1.5137	0.0046	18.9028	0.0571
5564	338	1.5741	0.0047	1.6487	0.0049	22.3085	0.0660
5565	362	1.7426	0.0048	1.7509	0.0048	23.2853	0.0644
5566	359	1.4633	0.0041	1.3776	0.0038	20.9939	0.0584
5567	338	1.2432	0.0037	1.2584	0.0037	16.5280	0.0489
5568	390	1.8080	0.0046	1.7903	0.0046	22.7614	0.0583
5569	317	1.2956	0.0041	1.3557	0.0043	17.3583	0.0548
5570	372	1.4747	0.0040	1.5660	0.0042	20.1889	0.0543
5571 TLLx	266	1.1965	0.0045	1.2383	0.0047	10.4273	0.0393
5572x NP		1.1060		1.0441		9.7488	
5573	339	1.3506	0.0040	1.3953	0.0041	15.7681	0.0465
5574	314	1.3576	0.0043	1.4521	0.0046	17.0319	0.0542

RATIO = ORGAN WEIGHT/BODY WEIGHT

NP=NOT PREGNANT

x=EXCLUDED FROM MEAN

	Individual Animal Gross and Microscopic Observations – F ₀ Generation	Appendix BB
--	---	-------------

Corresponding dose levels for each group were as follows:

Group 1 - 0 mg/kg/day
Group 2 - 64 mg/kg/day
Group 3 - 160 mg/kg/day
Group 4 - 400 mg/kg/day
Group 5 - 1000 mg/kg/day

Key to Abbreviations

Fallop = Fallopian tubes

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 1063
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 1
Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Left Epididymis Left Testis Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 1064
PHASE DAY OF DEATH: 64 PHASE: Dosing phase GROUP: 1

Tissue Gross Observations/Comments Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.

The following tissues were unremarkable microscopically:

Left Epididymis Parathyroid Left Testis Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice PHASE DAY OF DEATH: 64	SEX: Male PHASE: Dosing phase	ANIMAL: 1065 GROUP: 1.
Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.
Skin (other)	Sore, Cervical, Red, 1.6 - 1.9 cm Scab, Cervical, Red, 1.0 - 1.5 cm/ Surrounding sore	No micropathology observations on tissue.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Left Epididymis Left Testis Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 1066
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Left Epididymis Left Testis Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 1067
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 1
Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Left Epididymis Parathyroid Left Testis Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

-----		ANIMAL: 1068
STATUS: Final phase sacrifice	SEX: Male	
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Left Epididymis Left Testis Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 1069
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 1
Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Left Epididymis Parathyroid Left Testis Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 1070
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
--------	-----------------------------	-----------------------------------

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Left Epididymis Parathyroid Left Testis Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 1071
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 1
Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Left Epididymis Parathyroid Left Testis Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 1072
PHASE DAY OF DEATH: 64 PHASE: Dosing phase GROUP: 1

Tissue Gross Observations/Comments Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Left Epididymis Parathyroid Left Testis Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 1073
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Thyroid	No gross observations on tissue.	ECTOPIC THYMIC TISSUE, Present.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Left Epididymis Parathyroid Left Testis

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 1074
PHASE DAY OF DEATH: 64 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
 Left Epididymis Left Testis Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 2063
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 2
Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 2064
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 2
Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 2065
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 2

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
--------	-----------------------------	-----------------------------------

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Huntingdon Life Sciences, Inc. 034254

Page: 388

TBA

Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 2066
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 2

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
--------	-----------------------------	-----------------------------------

Tissues without comment under Gross Observations were within normal limits at necropsy. The following tissues were unremarkable microscopically:

 No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 2067
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 2
Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 2068
PHASE DAY OF DEATH: 64 PHASE: Dosing phase GROUP: 2

Tissue Gross Observations/Comments Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
 No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 2069
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 2
Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 2070
PHASE DAY OF DEATH: 64 PHASE: Dosing phase GROUP: 2

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Skin (other)	Hair Thin/Absent/ Extremities/ snout	No micropathology observations on tissue.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
 No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 2071
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 2
Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Page: 394

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 2072
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 2

Tissues without comment under Gross Observations were within normal limits at necropsy. The following tissues were unremarkable microscopically:

No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 2073
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 2
Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 2074
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 2
Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 3063
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 3
Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 3064
PHASE DAY OF DEATH: 64 PHASE: Dosing phase GROUP: 3

Tissue Gross Observations/Comments Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
 No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 3065
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 3
Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 3066
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 3
Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 3067
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 3
Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 3068
PHASE DAY OF DEATH: 64 PHASE: Dosing phase GROUP: 3

Tissue Gross Observations/Comments Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
 No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 3069
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 3.
Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 3070
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 3
Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 3071
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 3

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
--------	-----------------------------	-----------------------------------

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 3072
PHASE DAY OF DEATH: 64 PHASE: Dosing phase GROUP: 3

Tissue Gross Observations/Comments Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
 No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 3073
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 3
Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

06-Feb-04; 10:59
Huntingdon Life Sciences, Inc. 034254

Page: 408

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 3074
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 3
Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 4063
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 4
Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 4064
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 4
Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 4065
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 4
Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

06-Feb-04; 10:59
Huntingdon Life Sciences, Inc. 034254

Page: 412

TEA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice		SEX: Male	ANIMAL: 4066
PHASE DAY OF DEATH: 64		PHASE: Dosing phase	GROUP: 4
Tissue	Gross Observations/Comments	Microscopic Observations/Comments	

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 4067
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
--------	-----------------------------	-----------------------------------

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 4068
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
--------	-----------------------------	-----------------------------------

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 4069
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 4
Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Page: 416

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 4070
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 4

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

-----		-----	
STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 4071	
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 4	
-----		-----	
Tissue	Gross Observations/Comments	Microscopic Observations/Comments	
-----		-----	
Kidneys	Dilated Pelvis, Right, Moderate	No micropathology observations on tissue.	

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 4072
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
--------	-----------------------------	-----------------------------------

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 4073
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 4
Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 4074
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 4
Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 5063
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 5

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
--------	-----------------------------	-----------------------------------

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Left Epididymis Parathyroid Left Testis Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 5064
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 5

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.
Skin (other)	Hair Thin/Absent/ Extremities/ snout	No micropathology observations on tissue.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Left Epididymis Left Testis Thyroid

06-Feb-04; 10:59
Huntingdon Life Sciences, Inc. 034254

Page: 423

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 5065
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 5

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Left Epididymis Left Testis Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 5066
PHASE DAY OF DEATH: 64 PHASE: Dosing phase GROUP: 5

Tissue Gross Observations/Comments Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.

The following tissues were unremarkable microscopically:

Left Epididymis Parathyroid Left Testis Thyroid

06-Feb-04; 10:59
Huntingdon Life Sciences, Inc. 034254

Page: 425

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 5067
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 5

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
--------	-----------------------------	-----------------------------------

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Left Epididymis Parathyroid Left Testis Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 5068
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 5

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Left Epididymis Left Testis Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 5069
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 5

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Left Epididymis Left Testis Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

-----		-----	
STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 5070	
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 5	
-----		-----	
Tissue	Gross Observations/Comments	Microscopic Observations/Comments	
-----		-----	
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.	

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Left Epididymis Left Testis Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 5071
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 5
Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Left Epididymis Left Testis Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 5072
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 5

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Left Epididymis Left Testis Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

-----		-----	
STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 5073	
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 5	
-----		-----	
Tissue	Gross Observations/Comments	Microscopic Observations/Comments	

Left Testis	No gross observations on tissue.	TUBULAR DEGENERATION/ATROPHY, Slight.	

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Left Epididymis Parathyroid Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 5074
PHASE DAY OF DEATH: 64	PHASE: Dosing phase	GROUP: 5

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
--------	-----------------------------	-----------------------------------

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Left Epididymis Parathyroid Left Testis Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 1563
PHASE DAY OF DEATH: 72	PHASE: Dosing phase	GROUP: 1
Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Oviducts/Fallop Ovaries Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 1564
PHASE DAY OF DEATH: 78	PHASE: Dosing phase	GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Oviducts/Fallop Ovaries Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 1565
PHASE DAY OF DEATH: 72	PHASE: Dosing phase	GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Oviducts/Fallop Ovaries Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 1566
PHASE DAY OF DEATH: 74	PHASE: Dosing phase	GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
--------	-----------------------------	-----------------------------------

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Oviducts/Fallop Ovaries Parathyroid Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 1567
PHASE DAY OF DEATH: 55	PHASE: Dosing phase	GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Uterus	Cyst, Cervix, Clear/ Thick material, 1.5 X 1.0 cm Abnormal Contents, Bilateral horns, Clear, Slight/ Thick material	No micropathology observations on tissue.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Oviducts/Fallop Ovaries Parathyroid Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 1568
PHASE DAY OF DEATH: 72	PHASE: Dosing phase	GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
--------	-----------------------------	-----------------------------------

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Oviducts/Fallop Ovaries Parathyroid Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 1569
PHASE DAY OF DEATH: 73	PHASE: Dosing phase	GROUP: 1
Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Oviducts/Fallop Ovaries Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 1570
PHASE DAY OF DEATH: 72	PHASE: Dosing phase	GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.
Skin (other)	Hair Thin/Absent/ Extremities/ snout	No micropathology observations on tissue.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Oviducts/Fallop Ovaries Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 1571
PHASE DAY OF DEATH: 74	PHASE: Dosing phase.	GROUP: 1
Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
 Oviducts/Fallop Ovaries Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice		SEX: Female	ANIMAL: 1572
PHASE DAY OF DEATH: 75		PHASE: Dosing phase	GROUP: 1
Tissue	Gross Observations/Comments	Microscopic Observations/Comments	
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.	

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Oviducts/Fallop Ovaries Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 1573
PHASE DAY OF DEATH: 72	PHASE: Dosing phase	GROUP: 1
Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Oviducts/Fallop Ovaries Parathyroid Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 1574
PHASE DAY OF DEATH: 74	PHASE: Dosing phase	GROUP: 1
Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Oviducts/Fallop Ovaries Parathyroid Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 2563
PHASE DAY OF DEATH: 73 PHASE: Dosing phase GROUP: 2

Tissue Gross Observations/Comments Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
 No tissues examined.

06-Feb-04; 10:59
Huntingdon Life Sciences, Inc. 034254

Page: 446

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 2564
PHASE DAY OF DEATH: 77 PHASE: Dosing phase .GROUP: 2

Tissue Gross Observations/Comments Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
 No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 2565
PHASE DAY OF DEATH: 72	PHASE: Dosing phase	GROUP: 2
Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 2566
PHASE DAY OF DEATH: 71	PHASE: Dosing phase	GROUP: 2

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Tail	Scab, Distal, Brown, Moderate/ 0.6 - 0.9 cm	No micropathology observations on tissue.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 2567
PHASE DAY OF DEATH: 75	PHASE: Dosing phase	GROUP: 2

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
--------	-----------------------------	-----------------------------------

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 2568
PHASE DAY OF DEATH: 75 PHASE: Dosing phase GROUP: 2

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Uterus	Mass, Right horn, Tan, Firm/ 0.5 cm dia	No micropathology observations on tissue.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 2569
PHASE DAY OF DEATH: 74	PHASE: Dosing phase	GROUP: 2

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
--------	-----------------------------	-----------------------------------

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 2570
PHASE DAY OF DEATH: 71 PHASE: Dosing phase GROUP: 2

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Skin (other)	Hair Thin/Absent, Hindlegs, Moderate/ Extremities/ snout	No micropathology observations on tissue.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
 No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 2571
PHASE DAY OF DEATH: 75 PHASE: Dosing phase GROUP: 2

Tissue Gross Observations/Comments Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
 No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 2572
PHASE DAY OF DEATH: 56	PHASE: Dosing phase	GROUP: 2

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
--------	-----------------------------	-----------------------------------

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 2573
PHASE DAY OF DEATH: 73	PHASE: Dosing phase	GROUP: 2
Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 2574
PHASE DAY OF DEATH: 74	PHASE: Dosing phase	GROUP: 2

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
--------	-----------------------------	-----------------------------------

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

06-Feb-04; 10:59
Huntingdon Life Sciences, Inc. 034254

Page: 457

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 3563
PHASE DAY OF DEATH: 73	PHASE: Dosing phase	GROUP: 3
Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 3564
PHASE DAY OF DEATH: 72	PHASE: Dosing phase	GROUP: 3

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
--------	-----------------------------	-----------------------------------

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 3565
PHASE DAY OF DEATH: 80	PHASE: Dosing phase	GROUP: 3

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Lungs	Discolored, All lobes, Red, Foci, Slight/ 0.2 cm dia	No micropathology observations on tissue.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 3566
PHASE DAY OF DEATH: 76 PHASE: Dosing phase GROUP: 3

Tissue Gross Observations/Comments Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
 No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 3567
PHASE DAY OF DEATH: 72	PHASE: Dosing phase	GROUP: 3
Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 3568
PHASE DAY OF DEATH: 73 PHASE: Dosing phase GROUP: 3

Tissue Gross Observations/Comments Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
 No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 3569
PHASE DAY OF DEATH: 74	PHASE: Dosing phase	GROUP: 3

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
--------	-----------------------------	-----------------------------------

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 3570
PHASE DAY OF DEATH: 75	PHASE: Dosing phase	GROUP: 3

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
--------	-----------------------------	-----------------------------------

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

06-Feb-04; 10:59
Huntingdon Life Sciences, Inc. 034254

Page: 465

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 3571
PHASE DAY OF DEATH: 75	PHASE: Dosing phase	GROUP: 3

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
--------	-----------------------------	-----------------------------------

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
 No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 3572
PHASE DAY OF DEATH: 73	PHASE: Dosing phase	GROUP: 3
Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 3573
PHASE DAY OF DEATH: 76	PHASE: Dosing phase	GROUP: 3
Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 3574
PHASE DAY OF DEATH: 72	PHASE: Dosing phase	GROUP: 3

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
--------	-----------------------------	-----------------------------------

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 4563
PHASE DAY OF DEATH: 73	PHASE: Dosing phase	GROUP: 4
Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 4564
PHASE DAY OF DEATH: 75	PHASE: Dosing phase	GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Skin (other)	Mass, Tan, 0.2 - 0.5 cm, Firm/ bottom lip, right	No micropathology observations on tissue.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 4565
PHASE DAY OF DEATH: 74	PHASE: Dosing phase	GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Lungs	Discolored, All lobes, Red, Foci, Slight/ 0.2 cm dia	No micropathology observations on tissue.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

06-Feb-04; 10:59
Huntingdon Life Sciences, Inc. 034254

Page: 472

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 4566
PHASE DAY OF DEATH: 75	PHASE: Dosing phase	GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
--------	-----------------------------	-----------------------------------

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 4567
PHASE DAY OF DEATH: 75	PHASE: Dosing phase	GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
--------	-----------------------------	-----------------------------------

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 4568
PHASE DAY OF DEATH: 76 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Lungs	Discolored, Red, Focus, Slight/ Apical and cardiac lobes, 0.1 cm dia	No micropathology observations on tissue.
Skin (other)	Hair Thin/Absent/ Extremities/ snout	No micropathology observations on tissue.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 4569
PHASE DAY OF DEATH: 73	PHASE: Dosing phase	GROUP: 4
Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Page: 476

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 4570
PHASE DAY OF DEATH: 75	PHASE: Dosing phase	GROUP: 4

Tissues without comment under Gross Observations were within normal limits at necropsy. The following tissues were unremarkable microscopically:

No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 4571
PHASE DAY OF DEATH: 75	PHASE: Dosing phase	GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Lungs	Discolored, Red, Focus, Slight/ Apical lobe, 0.2 cm dia	No micropathology observations on tissue.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 4572
PHASE DAY OF DEATH: 75.	PHASE: Dosing phase	GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Kidneys	Dilated Pelvis, Bilateral, Slight	No micropathology observations on tissue.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice		SEX: Female	ANIMAL: 4573
PHASE DAY OF DEATH: 74		PHASE: Dosing phase	GROUP: 4
Tissue	Gross Observations/Comments	Microscopic Observations/Comments	

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 4574
PHASE DAY OF DEATH: 75 PHASE: Dosing phase GROUP: 4

Tissue Gross Observations/Comments Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
 No tissues examined.

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 5563
PHASE DAY OF DEATH: 75 PHASE: Dosing phase GROUP: 5

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Oviducts/Fallop Ovaries Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 5564
PHASE DAY OF DEATH: 73	PHASE: Dosing phase	GROUP: 5
Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Oviducts/Fallop Ovaries Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 5565
PHASE DAY OF DEATH: 76	PHASE: Dosing phase	GROUP: 5

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Kidneys	Dilated Pelvis, Right, Slight	No micropathology observations on tissue.
Lungs	Discolored, Red, Foci, Slight/ Left, 0.1 cm dia	No micropathology observations on tissue.
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Oviducts/Fallop Ovaries Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	
PHASE DAY OF DEATH: 77	PHASE: Dosing phase	

Tissue	Gross Observations/Comments	ANIMAL: 5566
		GROUP: 5
-----		-----
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.

Skin (other)	Hair Thin/Absent/ Extremities/ snout	No micropathology observations on tissue.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Oviducts/Fallop Ovaries Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 5567
PHASE DAY OF DEATH: 75	PHASE: Dosing phase	GROUP: 5
Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Oviducts/Fallop Ovaries Parathyroid Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 5568
PHASE DAY OF DEATH: 74	PHASE: Dosing phase	GROUP: 5

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Oviducts/Fallop Ovaries Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 5569
PHASE DAY OF DEATH: 75	PHASE: Dosing phase	GROUP: 5

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
--------	-----------------------------	-----------------------------------

Tissues without comment under Gross Observations were within normal limits at necropsy.

The following tissues were unremarkable microscopically:

Oviducts/Fallop Ovaries Parathyroid Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 5570
PHASE DAY OF DEATH: 72	PHASE: Dosing phase	GROUP: 5
Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Oviducts/Fallop Ovaries Parathyroid Thyroid

Page : 489

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 5571
PHASE DAY OF DEATH: 63	PHASE: Dosing phase	GROUP: 5.

Tissues without comment under Gross Observations were within normal limits at necropsy. The following tissues were unremarkable microscopically:

Oviducts/Fallop	Ovaries	Thyroid
-----------------	---------	---------

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 5572
PHASE DAY OF DEATH: 58	PHASE: Dosing phase	GROUP: 5

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Oviducts/Fallop Ovaries Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 5573
PHASE DAY OF DEATH: 75	PHASE: Dosing phase	GROUP: 5
Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Oviducts/Fallop Ovaries Thyroid

TBA
Reproduction/Developmental Toxicity Screening Test in Rats
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 5574
PHASE DAY OF DEATH: 73	PHASE: Dosing phase	GROUP: 5

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
--------	-----------------------------	-----------------------------------

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Oviducts/Fallop Ovaries Parathyroid Thyroid

	Individual Pup Necropsy Observations F ₁ Generation	Appendix CC
--	---	-------------

Key to Abbreviations

M	=	Malformation
V	=	Variation

APPENDIX CC - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 1 0 MG/KG/DAY

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
1563	1M	C	4	STOMACH	NO MILK IN STOMACH
	2M	K	21		NO REMARKABLE OBSERVATIONS
	3M	K	21		NO REMARKABLE OBSERVATIONS
	4M	C	4	STOMACH	NO MILK IN STOMACH
	5M	K	23		NO REMARKABLE OBSERVATIONS
	6M	K	21		NO REMARKABLE OBSERVATIONS
	9F	K	23		NO REMARKABLE OBSERVATIONS
	10F	K	21		NO REMARKABLE OBSERVATIONS
	11F	C	4		NO REMARKABLE OBSERVATIONS
	12F	K	21		NO REMARKABLE OBSERVATIONS
	13F	C	4	STOMACH	NO MILK IN STOMACH
	14F	K	21		NO REMARKABLE OBSERVATIONS
1564	1M	S		LUNGS STOMACH	FLOATATION TEST - STILLBORN NO MILK IN STOMACH
	2M	C	4		NO REMARKABLE OBSERVATIONS
	3M	C	4		NO REMARKABLE OBSERVATIONS
	4M	K	21		NO REMARKABLE OBSERVATIONS
	5M	K	21		NO REMARKABLE OBSERVATIONS
	6M	K	21		NO REMARKABLE OBSERVATIONS
	7M	K	23		NO REMARKABLE OBSERVATIONS
	8M	C	4		NO REMARKABLE OBSERVATIONS
	9M	C	4		NO REMARKABLE OBSERVATIONS
	10M	D	3	STOMACH	MILK IN STOMACH
	12F	K	21		NO REMARKABLE OBSERVATIONS
	13F	C	4		NO REMARKABLE OBSERVATIONS
	14F	K	21		NO REMARKABLE OBSERVATIONS
	15F	K	21		NO REMARKABLE OBSERVATIONS
	16F	K	23		NO REMARKABLE OBSERVATIONS
1565	3M	K	21		NO REMARKABLE OBSERVATIONS
	4M	C	4		NO REMARKABLE OBSERVATIONS
	5M	C	4		NO REMARKABLE OBSERVATIONS
	6M	K	21		NO REMARKABLE OBSERVATIONS
	7M	K	23		NO REMARKABLE OBSERVATIONS

SEX CODES: M=Male, F=Female, U=Undetermined

PUP STATUS CODES: S-STILLBORN D-DIED C-CULLED K-SCHEDULED SACRIFICE

APPENDIX CC - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 1 0 MG/KG/DAY

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
1565	(CONTINUED)				
	8M	K	21		NO REMARKABLE OBSERVATIONS
	9F	K	23		NO REMARKABLE OBSERVATIONS
	10F	K	21		NO REMARKABLE OBSERVATIONS
	11F	C	4		NO REMARKABLE OBSERVATIONS
	12F	K	21		NO REMARKABLE OBSERVATIONS
	13F	C	4		NO REMARKABLE OBSERVATIONS
	14F	C	4	STOMACH	NO MILK IN STOMACH
	15F	K	21		NO REMARKABLE OBSERVATIONS
1566	1F	S		LUNGS STOMACH	FLOATATION TEST - STILLBORN NO MILK IN STOMACH
	2M	K	21		NO REMARKABLE OBSERVATIONS
	3M	C	4	STOMACH	NO MILK IN STOMACH
	4M	C	4	STOMACH	NO MILK IN STOMACH
	5M	K	23		NO REMARKABLE OBSERVATIONS
	6M	K	21		NO REMARKABLE OBSERVATIONS
	7M	C	4		NO REMARKABLE OBSERVATIONS
	8M	C	4		NO REMARKABLE OBSERVATIONS
	9M	C	4		NO REMARKABLE OBSERVATIONS
	10M	C	4	STOMACH	NO MILK IN STOMACH
	11M	C	4	STOMACH	NO MILK IN STOMACH
	12M	K	21		NO REMARKABLE OBSERVATIONS
	14F	K	23		NO REMARKABLE OBSERVATIONS
	15F	K	21		NO REMARKABLE OBSERVATIONS
	16F	K	21		NO REMARKABLE OBSERVATIONS
	17F	C	4		NO REMARKABLE OBSERVATIONS
	18F	K	21		NO REMARKABLE OBSERVATIONS
1568	1M	C	4		NO REMARKABLE OBSERVATIONS
	2M	C	4		NO REMARKABLE OBSERVATIONS
	4M	K	23		NO REMARKABLE OBSERVATIONS
	5M	K	21		NO REMARKABLE OBSERVATIONS
	6M	K	21		NO REMARKABLE OBSERVATIONS
	7M	K	21		NO REMARKABLE OBSERVATIONS
	8M	C	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined

PUP STATUS CODES: S-STILLBORN C-CULLED K-SCHEDULED SACRIFICE

APPENDIX CC - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 1 0 MG/KG/DAY

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
1568	(CONTINUED)				
	10F	K	23		NO REMARKABLE OBSERVATIONS
	11F	K	21		NO REMARKABLE OBSERVATIONS
	12F	C	4		NO REMARKABLE OBSERVATIONS
	13F	K	21		NO REMARKABLE OBSERVATIONS
	14F	K	21		NO REMARKABLE OBSERVATIONS
1569	1M	D	0	LUNGS	FLOATATION TEST - FOUND DEAD
				STOMACH	NO MILK IN STOMACH
	2M	K	21		NO REMARKABLE OBSERVATIONS
	3M	K	21		NO REMARKABLE OBSERVATIONS
	4M	K	21		NO REMARKABLE OBSERVATIONS
	5M	K	23		NO REMARKABLE OBSERVATIONS
	7F	K	23		NO REMARKABLE OBSERVATIONS
	8F	C	4		NO REMARKABLE OBSERVATIONS
	9F	C	4		NO REMARKABLE OBSERVATIONS
	10F	C	4		NO REMARKABLE OBSERVATIONS
	11F	C	4		NO REMARKABLE OBSERVATIONS
	12F	K	21		NO REMARKABLE OBSERVATIONS
	13F	K	21		NO REMARKABLE OBSERVATIONS
	14F	K	21		NO REMARKABLE OBSERVATIONS
	15F	C	4		NO REMARKABLE OBSERVATIONS
1570	1M	C	4		NO REMARKABLE OBSERVATIONS
	2M	C	4		NO REMARKABLE OBSERVATIONS
	4M	K	23		NO REMARKABLE OBSERVATIONS
	5M	K	21		NO REMARKABLE OBSERVATIONS
	6M	C	4		NO REMARKABLE OBSERVATIONS
	7M	K	21		NO REMARKABLE OBSERVATIONS
	8M	C	4	STOMACH	NO MILK IN STOMACH
	9M	C	4		NO REMARKABLE OBSERVATIONS
	10M	K	21		NO REMARKABLE OBSERVATIONS
	11F	C	4		NO REMARKABLE OBSERVATIONS
	12F	K	23		NO REMARKABLE OBSERVATIONS
	14F	K	21		NO REMARKABLE OBSERVATIONS
	15F	K	21		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined

PUP STATUS CODES: D-DIED C-CULLED K-SCHEDULED SACRIFICE

APPENDIX CC - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 1 0 MG/KG/DAY

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
1570	(CONTINUED)				
	16F	K	21		NO REMARKABLE OBSERVATIONS
1571	1F	S		LUNGS STOMACH	FLOATATION TEST - STILLBORN NO MILK IN STOMACH
	2M	C	4		NO REMARKABLE OBSERVATIONS
	3M	K	21		NO REMARKABLE OBSERVATIONS
	4M	K	21		NO REMARKABLE OBSERVATIONS
	5M	C	4		NO REMARKABLE OBSERVATIONS
	6M	K	21		NO REMARKABLE OBSERVATIONS
	7M	C	4	STOMACH	NO MILK IN STOMACH
	8M	C	4		NO REMARKABLE OBSERVATIONS
	10M	K	23		NO REMARKABLE OBSERVATIONS
	11M	C	4	STOMACH	NO MILK IN STOMACH
	12F	K	21		NO REMARKABLE OBSERVATIONS
	13F	K	21		NO REMARKABLE OBSERVATIONS
	14F	K	21		NO REMARKABLE OBSERVATIONS
	15F	K	23		NO REMARKABLE OBSERVATIONS
1572	2M	K	23		NO REMARKABLE OBSERVATIONS
	3M	K	21		NO REMARKABLE OBSERVATIONS
	4M	C	4		NO REMARKABLE OBSERVATIONS
	5M	K	21		NO REMARKABLE OBSERVATIONS
	6M	C	4		NO REMARKABLE OBSERVATIONS
	7M	K	21		NO REMARKABLE OBSERVATIONS
	8F	K	21		NO REMARKABLE OBSERVATIONS
	9F	K	21		NO REMARKABLE OBSERVATIONS
	10F	C	4		NO REMARKABLE OBSERVATIONS
	11F	K	21		NO REMARKABLE OBSERVATIONS
	13F	C	4		NO REMARKABLE OBSERVATIONS
	14F	K	23		NO REMARKABLE OBSERVATIONS
	15F	C	4	STOMACH	NO MILK IN STOMACH
1573	1F	D	0	LUNGS STOMACH	FLOATATION TEST - FOUND DEAD NO MILK IN STOMACH
	2M	K	23		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined

PUP STATUS CODES: S-STILLBORN D-DIED C-CULLED K-SCHEDULED SACRIFICE

APPENDIX CC - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 1 0 MG/KG/DAY

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
1573	(CONTINUED)				
	3M	C	4		NO REMARKABLE OBSERVATIONS
	4M	K	21		NO REMARKABLE OBSERVATIONS
	5M	K	21		NO REMARKABLE OBSERVATIONS
	6M	K	21		NO REMARKABLE OBSERVATIONS
	7M	C	4	STOMACH	NO MILK IN STOMACH
	9F	C	4		NO REMARKABLE OBSERVATIONS
	10F	C	4	STOMACH	NO MILK IN STOMACH
	11F	K	21		NO REMARKABLE OBSERVATIONS
	12F	K	23		NO REMARKABLE OBSERVATIONS
	14F	K	21		NO REMARKABLE OBSERVATIONS
	15F	K	21		NO REMARKABLE OBSERVATIONS
1574	2M	K	21		NO REMARKABLE OBSERVATIONS
	3M	C	4	STOMACH	NO MILK IN STOMACH
	4M	K	21		NO REMARKABLE OBSERVATIONS
	5M	K	21		NO REMARKABLE OBSERVATIONS
	6M	C	4	STOMACH	NO MILK IN STOMACH
	7M	K	23		NO REMARKABLE OBSERVATIONS
	8F	K	21		NO REMARKABLE OBSERVATIONS
	9F	K	21		NO REMARKABLE OBSERVATIONS
	10F	K	21		NO REMARKABLE OBSERVATIONS
	11F	K	23		NO REMARKABLE OBSERVATIONS

SEX CODES: M=Male, F=Female, U=Undetermined

PUP STATUS CODES: C-CULLED K-SCHEDULED SACRIFICE

APPENDIX CC - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 2 64 MG/KG/DAY

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
2563	1M	K	21		NO REMARKABLE OBSERVATIONS
	2M	K	21		NO REMARKABLE OBSERVATIONS
	3M	C	4		NO REMARKABLE OBSERVATIONS
	4M	K	23		NO REMARKABLE OBSERVATIONS
	5M	K	21		NO REMARKABLE OBSERVATIONS
	7F	C	4		NO REMARKABLE OBSERVATIONS
	8F	C	4	STOMACH	NO MILK IN STOMACH
	10F	C	4		NO REMARKABLE OBSERVATIONS
	11F	K	21		NO REMARKABLE OBSERVATIONS
	12F	K	21		NO REMARKABLE OBSERVATIONS
	13F	K	21		NO REMARKABLE OBSERVATIONS
	14F	C	4		NO REMARKABLE OBSERVATIONS
	15F	C	4		NO REMARKABLE OBSERVATIONS
	16F	K	23		NO REMARKABLE OBSERVATIONS
2564	1M	K	21		NO REMARKABLE OBSERVATIONS
	2M	K	21		NO REMARKABLE OBSERVATIONS
	4M	K	23		NO REMARKABLE OBSERVATIONS
	6F	K	21		NO REMARKABLE OBSERVATIONS
	7F	K	23		NO REMARKABLE OBSERVATIONS
	8F	C	4		NO REMARKABLE OBSERVATIONS
	9F	C	4		NO REMARKABLE OBSERVATIONS
	10F	K	21		NO REMARKABLE OBSERVATIONS
	11F	C	4		NO REMARKABLE OBSERVATIONS
	12F	K	21		NO REMARKABLE OBSERVATIONS
	13F	K	21		NO REMARKABLE OBSERVATIONS
2565	1M	K	21		NO REMARKABLE OBSERVATIONS
	2M	K	21		NO REMARKABLE OBSERVATIONS
	3M	K	21		NO REMARKABLE OBSERVATIONS
	4M	C	4		NO REMARKABLE OBSERVATIONS
	5M	K	23		NO REMARKABLE OBSERVATIONS
	6M	C	4		NO REMARKABLE OBSERVATIONS
	7M	C	4		NO REMARKABLE OBSERVATIONS
	8M	C	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined

PUP STATUS CODES: C-CULLED K-SCHEDULED SACRIFICE

APPENDIX CC - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 2 64 MG/KG/DAY

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
2565	(CONTINUED)				
	9M	C	4		NO REMARKABLE OBSERVATIONS
	11F	K	21		NO REMARKABLE OBSERVATIONS
	12F	K	21		NO REMARKABLE OBSERVATIONS
	13F	K	21		NO REMARKABLE OBSERVATIONS
	14F	K	23		NO REMARKABLE OBSERVATIONS
2566	1M	K	23		NO REMARKABLE OBSERVATIONS
	2M	K	21	KIDNEY	V DILATED RENAL PELVIS (PAPILLA REDUCED); MODERATE; RIGHT TISSUE SAVED
	4M	K	21		NO REMARKABLE OBSERVATIONS
	5M	C	4		NO REMARKABLE OBSERVATIONS
	6M	K	21		NO REMARKABLE OBSERVATIONS
	7F	K	21		NO REMARKABLE OBSERVATIONS
	8F	C	4		NO REMARKABLE OBSERVATIONS
	9F	C	4		NO REMARKABLE OBSERVATIONS
	10F	K	21		NO REMARKABLE OBSERVATIONS
	11F	K	21		NO REMARKABLE OBSERVATIONS
	13F	K	23		NO REMARKABLE OBSERVATIONS
2567	1M	C	4		NO REMARKABLE OBSERVATIONS
	2M	K	21	THORACIC CAVITY	MASS; RIGHT DIAPHRAGM-0.8 CM IN DIAMETER, TAN, FIRM TISSUE SAVED
	3M	K	21		NO REMARKABLE OBSERVATIONS
	5M	K	23		NO REMARKABLE OBSERVATIONS
	6M	K	21		NO REMARKABLE OBSERVATIONS
	7M	K	21		NO REMARKABLE OBSERVATIONS
	8M	C	4		NO REMARKABLE OBSERVATIONS
	9F	K	21		NO REMARKABLE OBSERVATIONS
	10F	K	23		NO REMARKABLE OBSERVATIONS
	11F	K	21		NO REMARKABLE OBSERVATIONS
	13F	D	2	STOMACH	MILK IN STOMACH

SEX CODES: M=Male, F=Female, U=Undetermined

PUP STATUS CODES: D-DIED C-CULLED K-SCHEDULED SACRIFICE

APPENDIX CC - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 2 64 MG/KG/DAY

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
2568	1M	D	0	LUNGS	FLOATATION TEST - FOUND DEAD
				STOMACH	MILK IN STOMACH
	2M	S		LUNGS	FLOATATION TEST - STILLBORN
				STOMACH	NO MILK IN STOMACH
	4M	K	23	LUNGS	FLUID-FILLED; SLIGHT
					ALL LOBES, WHITE FROTHY FLUID
					TISSUE SAVED
	5M	K	21		NO REMARKABLE OBSERVATIONS
	6M	K	21		NO REMARKABLE OBSERVATIONS
	7M	K	21		NO REMARKABLE OBSERVATIONS
	8M	K	21		NO REMARKABLE OBSERVATIONS
	9M	C	4		NO REMARKABLE OBSERVATIONS
	10M	C	4		NO REMARKABLE OBSERVATIONS
	11M	C	4		NO REMARKABLE OBSERVATIONS
2569	12F	K	21		NO REMARKABLE OBSERVATIONS
	13F	K	23		NO REMARKABLE OBSERVATIONS
	14F	K	21		NO REMARKABLE OBSERVATIONS
	1M	C	4		NO REMARKABLE OBSERVATIONS
	2M	K	21	EXTERNAL EXAM	ALOPECIA - EXTREMITIES/SNOUT
					EXTERNAL FINDING CONFIRMED
	4M	K	21		NO REMARKABLE OBSERVATIONS
	5M	K	21	EXTERNAL EXAM	ALOPECIA - EXTREMITIES/SNOUT
					EXTERNAL FINDING CONFIRMED
	6M	K	23		NO REMARKABLE OBSERVATIONS
	8F	K	21	EXTERNAL EXAM	ALOPECIA - EXTREMITIES/SNOUT
					EXTERNAL FINDING CONFIRMED
	9F	C	4		NO REMARKABLE OBSERVATIONS
	10F	C	4	STOMACH	NO MILK IN STOMACH
	11F	C	4	STOMACH	NO MILK IN STOMACH
	12F	K	21	EXTERNAL EXAM	ALOPECIA - EXTREMITIES/SNOUT
					EXTERNAL FINDING CONFIRMED
	13F	K	21	EXTERNAL EXAM	ALOPECIA - EXTREMITIES/SNOUT
					EXTERNAL FINDING CONFIRMED
	14F	C	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined

PUP STATUS CODES: S-STILLBORN D-DIED C-CULLED K-SCHEDULED SACRIFICE

APPENDIX CC - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 2 64 MG/KG/DAY

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
2569	(CONTINUED)				
	15F	K	23	EXTERNAL EXAM	ALOPECIA - EXTREMITIES/SNOUT EXTERNAL FINDING NOT CONFIRMED
2570	1M	K	21		NO REMARKABLE OBSERVATIONS
	2M	K	21		NO REMARKABLE OBSERVATIONS
	4M	K	21		NO REMARKABLE OBSERVATIONS
	5M	K	23		NO REMARKABLE OBSERVATIONS
	6M	C	4		NO REMARKABLE OBSERVATIONS
	7M	C	4		NO REMARKABLE OBSERVATIONS
	8F	K	21		NO REMARKABLE OBSERVATIONS
	9F	K	21		NO REMARKABLE OBSERVATIONS
	10F	K	21		NO REMARKABLE OBSERVATIONS
	11F	K	23		NO REMARKABLE OBSERVATIONS
	12F	C	4		NO REMARKABLE OBSERVATIONS
	13F	C	4		NO REMARKABLE OBSERVATIONS
2571	2M	C	4		NO REMARKABLE OBSERVATIONS
	3M	K	21		NO REMARKABLE OBSERVATIONS
	4M	C	4		NO REMARKABLE OBSERVATIONS
	5M	C	4		NO REMARKABLE OBSERVATIONS
	6M	C	4		NO REMARKABLE OBSERVATIONS
	7M	K	21		NO REMARKABLE OBSERVATIONS
	8M	K	21		NO REMARKABLE OBSERVATIONS
	9M	K	23		NO REMARKABLE OBSERVATIONS
	10F	K	21		NO REMARKABLE OBSERVATIONS
	11F	K	23		NO REMARKABLE OBSERVATIONS
	12F	C	4		NO REMARKABLE OBSERVATIONS
	14F	K	21		NO REMARKABLE OBSERVATIONS
	15F	C	4		NO REMARKABLE OBSERVATIONS
	16F	K	21		NO REMARKABLE OBSERVATIONS
2573	1M	C	4		NO REMARKABLE OBSERVATIONS
	2M	C	4		NO REMARKABLE OBSERVATIONS
	3M	C	4		NO REMARKABLE OBSERVATIONS
	4M	K	21		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F-Female, U=Undetermined

PUP STATUS CODES: C-CULLED K-SCHEDULED SACRIFICE

6-FEB-2004 11:20

Huntingdon Life Sciences 03-4254

PAGE 503

APPENDIX CC - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 2 64 MG/KG/DAY

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
2573	(CONTINUED)				
	5M	K	21		NO REMARKABLE OBSERVATIONS
	6M	K	21		NO REMARKABLE OBSERVATIONS
	7M	C	4		NO REMARKABLE OBSERVATIONS
	8M	K	23		NO REMARKABLE OBSERVATIONS
	9M	C	4	STOMACH	NO MILK IN STOMACH
	11F	K	21		NO REMARKABLE OBSERVATIONS
	12F	K	23		NO REMARKABLE OBSERVATIONS
	13F	K	21		NO REMARKABLE OBSERVATIONS
	14F	K	21		NO REMARKABLE OBSERVATIONS
2574	2M	K	23		NO REMARKABLE OBSERVATIONS
	3M	K	21		NO REMARKABLE OBSERVATIONS
	4M	K	21		NO REMARKABLE OBSERVATIONS
	5F	K	21		NO REMARKABLE OBSERVATIONS
	6F	K	21		NO REMARKABLE OBSERVATIONS
	8F	K	21		NO REMARKABLE OBSERVATIONS
	9F	K	23		NO REMARKABLE OBSERVATIONS

SEX CODES: M=Male, F=Female, U=Undetermined

PUP STATUS CODES: C-CULLED K-SCHEDULED SACRIFICE

APPENDIX CC - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 3 160 MG/KG/DAY

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
3563	1M	C	4		NO REMARKABLE OBSERVATIONS
	2M	K	21		NO REMARKABLE OBSERVATIONS
	3M	C	4		NO REMARKABLE OBSERVATIONS
	4M	C	4		NO REMARKABLE OBSERVATIONS
	5M	K	21		NO REMARKABLE OBSERVATIONS
	7M	K	21		NO REMARKABLE OBSERVATIONS
	8M	D	1	GROSS EXAM	AUTOLYSIS
	9M	K	23		NO REMARKABLE OBSERVATIONS
	10M	C	4		NO REMARKABLE OBSERVATIONS
	11M	C	4	STOMACH	NO MILK IN STOMACH
	12F	K	21		NO REMARKABLE OBSERVATIONS
	14F	C	4	STOMACH	NO MILK IN STOMACH
	15M	C	4	STOMACH	NO MILK IN STOMACH
	16F	C	4	STOMACH	NO MILK IN STOMACH
	17F	K	21		NO REMARKABLE OBSERVATIONS
	18F	K	21		NO REMARKABLE OBSERVATIONS
	19F	K	23		NO REMARKABLE OBSERVATIONS
3564	1M	C	4	STOMACH	NO MILK IN STOMACH
	2M	K	21		NO REMARKABLE OBSERVATIONS
	3M	K	21		NO REMARKABLE OBSERVATIONS
	4M	K	21		NO REMARKABLE OBSERVATIONS
	5M	K	23		NO REMARKABLE OBSERVATIONS
	7F	C	4		NO REMARKABLE OBSERVATIONS
	8F	K	21		NO REMARKABLE OBSERVATIONS
	9F	K	23		NO REMARKABLE OBSERVATIONS
	10F	K	21		NO REMARKABLE OBSERVATIONS
	12F	K	21		NO REMARKABLE OBSERVATIONS
	13F	C	4	STOMACH	NO MILK IN STOMACH
	14F	C	4	STOMACH	NO MILK IN STOMACH
	15F	C	4	STOMACH	NO MILK IN STOMACH
3565	1M	K	21		NO REMARKABLE OBSERVATIONS
	2M	K	21		NO REMARKABLE OBSERVATIONS
	4M	K	23		NO REMARKABLE OBSERVATIONS

SEX CODES: M=Male, F=Female, U=Undetermined

PUP STATUS CODES: D-DIED C-CULLED K-SCHEDULED SACRIFICE

APPENDIX CC - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 3 160 MG/KG/DAY

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
3565	(CONTINUED)				
	5M	C	4		NO REMARKABLE OBSERVATIONS
	6M	K	21		NO REMARKABLE OBSERVATIONS
	7F	C	4		NO REMARKABLE OBSERVATIONS
	8F	C	4		NO REMARKABLE OBSERVATIONS
	9F	K	23		NO REMARKABLE OBSERVATIONS
	11F	C	4		NO REMARKABLE OBSERVATIONS
	12F	K	21		NO REMARKABLE OBSERVATIONS
	13F	K	21		NO REMARKABLE OBSERVATIONS
	14F	K	21		NO REMARKABLE OBSERVATIONS
	15F	C	4		NO REMARKABLE OBSERVATIONS
3566	1M	C	4		NO REMARKABLE OBSERVATIONS
	2M	K	21		NO REMARKABLE OBSERVATIONS
	3M	K	21		NO REMARKABLE OBSERVATIONS
	5M	C	4		NO REMARKABLE OBSERVATIONS
	6M	K	23		NO REMARKABLE OBSERVATIONS
	7M	C	4		NO REMARKABLE OBSERVATIONS
	8M	C	4		NO REMARKABLE OBSERVATIONS
	9M	K	21		NO REMARKABLE OBSERVATIONS
	10M	K	21		NO REMARKABLE OBSERVATIONS
	11M	K	21		NO REMARKABLE OBSERVATIONS
	13F	K	23		NO REMARKABLE OBSERVATIONS
	14F	K	21		NO REMARKABLE OBSERVATIONS
3567	1M	K	21		NO REMARKABLE OBSERVATIONS
	2M	K	21		NO REMARKABLE OBSERVATIONS
	3M	K	21		NO REMARKABLE OBSERVATIONS
	5M	C	4		NO REMARKABLE OBSERVATIONS
	6M	K	23		NO REMARKABLE OBSERVATIONS
	8F	K	23		NO REMARKABLE OBSERVATIONS
	9F	K	21		NO REMARKABLE OBSERVATIONS
	10F	C	4	STOMACH	NO MILK IN STOMACH
	11F	K	21		NO REMARKABLE OBSERVATIONS
	12F	K	21		NO REMARKABLE OBSERVATIONS
	13F	C	4	STOMACH	NO MILK IN STOMACH

SEX CODES: M-Male, F=Female, U=Undetermined

PUP STATUS CODES: C-CULLED K-SCHEDULED SACRIFICE

APPENDIX CC - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 3 160 MG/KG/DAY

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
3567	(CONTINUED)				
	14F	C	4		NO REMARKABLE OBSERVATIONS
	15F	C	4		NO REMARKABLE OBSERVATIONS
	16F	C	4	STOMACH	NO MILK IN STOMACH
3568	1M	C	4	STOMACH	NO MILK IN STOMACH
	2M	K	21		NO REMARKABLE OBSERVATIONS
	3M	K	23		NO REMARKABLE OBSERVATIONS
	5M	K	21		NO REMARKABLE OBSERVATIONS
	6M	C	4		NO REMARKABLE OBSERVATIONS
	7M	K	21		NO REMARKABLE OBSERVATIONS
	8M	C	4		NO REMARKABLE OBSERVATIONS
	9M	C	4		NO REMARKABLE OBSERVATIONS
	11F	K	21		NO REMARKABLE OBSERVATIONS
	12F	K	21		NO REMARKABLE OBSERVATIONS
	13F	K	23		NO REMARKABLE OBSERVATIONS
	14F	K	21		NO REMARKABLE OBSERVATIONS
3569	1M	S		GROSS EXAM	CANNIBALIZED
	2U	S		GROSS EXAM	CANNIBALIZED
	3F	S		GROSS EXAM	CANNIBALIZED
	5F	K	28		NO REMARKABLE OBSERVATIONS
3570	1M	K	21		NO REMARKABLE OBSERVATIONS
	3M	K	21		NO REMARKABLE OBSERVATIONS
	4M	K	23		NO REMARKABLE OBSERVATIONS
	5M	K	21		NO REMARKABLE OBSERVATIONS
	6F	K	21		NO REMARKABLE OBSERVATIONS
	7F	K	21		NO REMARKABLE OBSERVATIONS
	8F	K	21		NO REMARKABLE OBSERVATIONS
	9F	C	4		NO REMARKABLE OBSERVATIONS
	10F	K	23		NO REMARKABLE OBSERVATIONS
3571	1U	S		GROSS EXAM	CANNIBALIZED
	3M	K	21		NO REMARKABLE OBSERVATIONS
	4M	K	21		NO REMARKABLE OBSERVATIONS

SEX CODES: M=Male, F=Female, U=Undetermined

PUP STATUS CODES: S-STILLBORN C-CULLED K-SCHEDULED SACRIFICE

APPENDIX CC - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 3 160 MG/KG/DAY

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
3571	(CONTINUED)				
	5M	C	4		NO REMARKABLE OBSERVATIONS
	6M	K	23		NO REMARKABLE OBSERVATIONS
	7M	K	21		NO REMARKABLE OBSERVATIONS
	8F	K	21		NO REMARKABLE OBSERVATIONS
	9F	K	21		NO REMARKABLE OBSERVATIONS
	10F	K	23		NO REMARKABLE OBSERVATIONS
	11F	C	4		NO REMARKABLE OBSERVATIONS
	12F	K	21		NO REMARKABLE OBSERVATIONS
	13F	C	4		NO REMARKABLE OBSERVATIONS
	14F	C	4		NO REMARKABLE OBSERVATIONS
3572	2M	K	23		NO REMARKABLE OBSERVATIONS
	3M	K	21		NO REMARKABLE OBSERVATIONS
	4M	C	4		NO REMARKABLE OBSERVATIONS
	5M	C	4		NO REMARKABLE OBSERVATIONS
	6M	K	21		NO REMARKABLE OBSERVATIONS
	7M	C	4		NO REMARKABLE OBSERVATIONS
	8M	C	4		NO REMARKABLE OBSERVATIONS
	9M	K	21		NO REMARKABLE OBSERVATIONS
	11F	C	4		NO REMARKABLE OBSERVATIONS
	12F	K	21		NO REMARKABLE OBSERVATIONS
	13F	K	23		NO REMARKABLE OBSERVATIONS
	14F	K	21		NO REMARKABLE OBSERVATIONS
	15F	K	21		NO REMARKABLE OBSERVATIONS
3573	1M	K	21	LUNGS	DISCOLORED FOCI; SLIGHT DIAPHRAGMATIC LOBE - 0.1 CM IN DIAMETER, RED TISSUE SAVED
				GONADS	M UNDESCENDED TESTE(S); RIGHT TISSUE SAVED
	4M	K	21		NO REMARKABLE OBSERVATIONS
	5M	K	21		NO REMARKABLE OBSERVATIONS
	6M	C	4		NO REMARKABLE OBSERVATIONS
	7M	K	23		NO REMARKABLE OBSERVATIONS
	8F	K	21		NO REMARKABLE OBSERVATIONS

SEX CODES: M=Male, F=Female, U=Undetermined

PUP STATUS CODES: C-CULLED K-SCHEDULED SACRIFICE

APPENDIX CC - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 3 160 MG/KG/DAY

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
3573	(CONTINUED)				
	9F	K	21		NO REMARKABLE OBSERVATIONS
	10F	C	4		NO REMARKABLE OBSERVATIONS
	11F	K	23		NO REMARKABLE OBSERVATIONS
	12F	C	4		NO REMARKABLE OBSERVATIONS
	13F	K	21		NO REMARKABLE OBSERVATIONS
	14F	C	4		NO REMARKABLE OBSERVATIONS
	15F	D	0	LUNGS	FLOATATION TEST - FOUND DEAD
				STOMACH	MILK IN STOMACH
	16F	C	4		NO REMARKABLE OBSERVATIONS
3574	2M	K	21		NO REMARKABLE OBSERVATIONS
	3M	K	21		NO REMARKABLE OBSERVATIONS
	4M	C	4	STOMACH	NO MILK IN STOMACH
	6M	K	23		NO REMARKABLE OBSERVATIONS
	7M	K	21		NO REMARKABLE OBSERVATIONS
	8M	C	4	STOMACH	NO MILK IN STOMACH
	9F	K	21		NO REMARKABLE OBSERVATIONS
	10F	K	23		NO REMARKABLE OBSERVATIONS
	11F	K	21		NO REMARKABLE OBSERVATIONS
	12F	K	21		NO REMARKABLE OBSERVATIONS
	13F	C	4	STOMACH	NO MILK IN STOMACH

SEX CODES: M-Male, F=Female, U=Undetermined

PUP STATUS CODES: D-DIED C-CULLED K-SCHEDULED SACRIFICE

APPENDIX CC - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 4 400 MG/KG/DAY

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
4563	1M	K	21		NO REMARKABLE OBSERVATIONS
	2M	K	21		NO REMARKABLE OBSERVATIONS
	3M	K	21		NO REMARKABLE OBSERVATIONS
	4M	C	4		NO REMARKABLE OBSERVATIONS
	5M	C	4		NO REMARKABLE OBSERVATIONS
	7M	K	23		NO REMARKABLE OBSERVATIONS
	9F	K	21		NO REMARKABLE OBSERVATIONS
	10F	C	4		NO REMARKABLE OBSERVATIONS
	11F	K	21		NO REMARKABLE OBSERVATIONS
	12F	K	21		NO REMARKABLE OBSERVATIONS
	13F	K	23		NO REMARKABLE OBSERVATIONS
4564	1M	K	23		NO REMARKABLE OBSERVATIONS
	2M	K	21		NO REMARKABLE OBSERVATIONS
	3M	K	21		NO REMARKABLE OBSERVATIONS
	4M	C	4		NO REMARKABLE OBSERVATIONS
	5M	K	21		NO REMARKABLE OBSERVATIONS
	6M	C	4		NO REMARKABLE OBSERVATIONS
	8M	C	4		NO REMARKABLE OBSERVATIONS
	10F	K	23		NO REMARKABLE OBSERVATIONS
	11F	K	21		NO REMARKABLE OBSERVATIONS
	12F	K	21		NO REMARKABLE OBSERVATIONS
	13F	C	4		NO REMARKABLE OBSERVATIONS
	14F	K	21		NO REMARKABLE OBSERVATIONS
	15F	C	4		NO REMARKABLE OBSERVATIONS
4565	1M	C	4		NO REMARKABLE OBSERVATIONS
	2M	C	4		NO REMARKABLE OBSERVATIONS
	3M	K	21		NO REMARKABLE OBSERVATIONS
	4M	K	21		NO REMARKABLE OBSERVATIONS
	6M	C	4	STOMACH	NO MILK IN STOMACH
	7M	C	4	STOMACH	NO MILK IN STOMACH
	8M	C	4		NO REMARKABLE OBSERVATIONS
	9M	K	21		NO REMARKABLE OBSERVATIONS
	10M	C	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M=Male, F=Female, U=Undetermined

PUP STATUS CODES: C-CULLED K-SCHEDULED SACRIFICE

APPENDIX CC - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 4 400 MG/KG/DAY

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
4565	(CONTINUED)				
	11M	K	23		NO REMARKABLE OBSERVATIONS
	13F	K	21		NO REMARKABLE OBSERVATIONS
	14F	K	21		NO REMARKABLE OBSERVATIONS
	16F	K	23		NO REMARKABLE OBSERVATIONS
	17F	C	4		NO REMARKABLE OBSERVATIONS
	18F	K	21		NO REMARKABLE OBSERVATIONS
4566	1M	C	4		NO REMARKABLE OBSERVATIONS
	2M	D	12	STOMACH	MILK IN STOMACH
	3M	K	21		NO REMARKABLE OBSERVATIONS
	4M	C	4		NO REMARKABLE OBSERVATIONS
	6M	K	23		NO REMARKABLE OBSERVATIONS
	7M	K	21		NO REMARKABLE OBSERVATIONS
	8F	K	23		NO REMARKABLE OBSERVATIONS
	9F	C	4		NO REMARKABLE OBSERVATIONS
	10F	C	4		NO REMARKABLE OBSERVATIONS
	12F	K	21		NO REMARKABLE OBSERVATIONS
	13F	K	21		NO REMARKABLE OBSERVATIONS
	14F	K	21		NO REMARKABLE OBSERVATIONS
4567	1M	K	21		NO REMARKABLE OBSERVATIONS
	2M	K	21		NO REMARKABLE OBSERVATIONS
	3M	C	4		NO REMARKABLE OBSERVATIONS
	4M	C	4		NO REMARKABLE OBSERVATIONS
	5M	C	4	STOMACH	NO MILK IN STOMACH
	6M	C	4		NO REMARKABLE OBSERVATIONS
	7M	K	21		NO REMARKABLE OBSERVATIONS
	9M	K	23		NO REMARKABLE OBSERVATIONS
	10F	K	23		NO REMARKABLE OBSERVATIONS
	12F	K	21		NO REMARKABLE OBSERVATIONS
	13F	K	21		NO REMARKABLE OBSERVATIONS
	14F	K	21		NO REMARKABLE OBSERVATIONS
	15F	C	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined

PUP STATUS CODES: D-DIED C-CULLED K-SCHEDULED SACRIFICE

APPENDIX CC - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 4 400 MG/KG/DAY

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
4568	1M	C	4		NO REMARKABLE OBSERVATIONS
	2M	C	4		NO REMARKABLE OBSERVATIONS
	3M	K	21		NO REMARKABLE OBSERVATIONS
	4M	K	21		NO REMARKABLE OBSERVATIONS
	5M	K	23		NO REMARKABLE OBSERVATIONS
	7M	C	4		NO REMARKABLE OBSERVATIONS
	8M	C	4		NO REMARKABLE OBSERVATIONS
	9M	K	21		NO REMARKABLE OBSERVATIONS
	11F	C	4		NO REMARKABLE OBSERVATIONS
	12F	K	21		NO REMARKABLE OBSERVATIONS
	13F	K	21		NO REMARKABLE OBSERVATIONS
	14F	K	21		NO REMARKABLE OBSERVATIONS
	15F	K	23		NO REMARKABLE OBSERVATIONS
	16F	C	4		NO REMARKABLE OBSERVATIONS
4569	1M	K	21		NO REMARKABLE OBSERVATIONS
	2M	C	4		NO REMARKABLE OBSERVATIONS
	3M	K	21		NO REMARKABLE OBSERVATIONS
	4M	K	23		NO REMARKABLE OBSERVATIONS
	6M	K	21		NO REMARKABLE OBSERVATIONS
	7F	K	21		NO REMARKABLE OBSERVATIONS
	8F	K	21		NO REMARKABLE OBSERVATIONS
	9F	K	21		NO REMARKABLE OBSERVATIONS
	10F	K	23		NO REMARKABLE OBSERVATIONS
	12F	S		LUNGS	FLOATATION TEST - STILLBORN
				STOMACH	NO MILK IN STOMACH
	13F	S		LUNGS	FLOATATION TEST - STILLBORN
				STOMACH	NO MILK IN STOMACH
	14F	S		LUNGS	FLOATATION TEST - STILLBORN
				STOMACH	NO MILK IN STOMACH
4570	1M	C	4		NO REMARKABLE OBSERVATIONS
	3M	K	23		NO REMARKABLE OBSERVATIONS
	4M	K	21		NO REMARKABLE OBSERVATIONS
	5M	K	21		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined

PUP STATUS CODES: S-STILLBORN C-CULLED K-SCHEDULED SACRIFICE

APPENDIX CC - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 4 400 MG/KG/DAY

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION

4570	(CONTINUED)				
	6M	K	21		NO REMARKABLE OBSERVATIONS
	7M	C	4		NO REMARKABLE OBSERVATIONS
	8F	K	21		NO REMARKABLE OBSERVATIONS
	9F	K	21		NO REMARKABLE OBSERVATIONS
	10F	K	21		NO REMARKABLE OBSERVATIONS
	11F	C	4		NO REMARKABLE OBSERVATIONS
	12F	C	4		NO REMARKABLE OBSERVATIONS
	14F	C	4		NO REMARKABLE OBSERVATIONS
	15F	C	4		NO REMARKABLE OBSERVATIONS
	16F	C	4		NO REMARKABLE OBSERVATIONS
	17F	K	23		NO REMARKABLE OBSERVATIONS
	18F	C	4	STOMACH	NO MILK IN STOMACH

4571	1M	K	21		NO REMARKABLE OBSERVATIONS
	2M	K	21		NO REMARKABLE OBSERVATIONS
	3M	K	23		NO REMARKABLE OBSERVATIONS
	4M	K	21		NO REMARKABLE OBSERVATIONS
	5M	K	21		NO REMARKABLE OBSERVATIONS
	7F	K	23		NO REMARKABLE OBSERVATIONS
	9F	K	21		NO REMARKABLE OBSERVATIONS
	10F	K	21		NO REMARKABLE OBSERVATIONS

4572	1M	K	21		NO REMARKABLE OBSERVATIONS
	2M	K	21		NO REMARKABLE OBSERVATIONS
	4M	K	21		NO REMARKABLE OBSERVATIONS
	5M	K	23		NO REMARKABLE OBSERVATIONS
	6F	K	21		NO REMARKABLE OBSERVATIONS
	7F	K	21		NO REMARKABLE OBSERVATIONS
	8F	K	21		NO REMARKABLE OBSERVATIONS
	10F	C	4		NO REMARKABLE OBSERVATIONS
	11F	C	4		NO REMARKABLE OBSERVATIONS
	12F	C	4		NO REMARKABLE OBSERVATIONS
	13F	K	23		NO REMARKABLE OBSERVATIONS

SEX CODES: M=Male, F=Female, U=Undetermined

PUP STATUS CODES: C-CULLED K-SCHEDULED SACRIFICE

APPENDIX CC - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 4 400 MG/KG/DAY

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
4573	1M	C	4		NO REMARKABLE OBSERVATIONS
	2M	C	4		NO REMARKABLE OBSERVATIONS
	3M	C	4		NO REMARKABLE OBSERVATIONS
	4M	C	4		NO REMARKABLE OBSERVATIONS
	6M	K	23		NO REMARKABLE OBSERVATIONS
	7M	K	21		NO REMARKABLE OBSERVATIONS
	8M	K	21		NO REMARKABLE OBSERVATIONS
	9M	C	4		NO REMARKABLE OBSERVATIONS
	10M	K	21		NO REMARKABLE OBSERVATIONS
	11F	K	21		NO REMARKABLE OBSERVATIONS
	12F	K	21		NO REMARKABLE OBSERVATIONS
	13F	K	23		NO REMARKABLE OBSERVATIONS
	14F	K	21		NO REMARKABLE OBSERVATIONS
4574	1M	K	21		NO REMARKABLE OBSERVATIONS
	2M	K	21		NO REMARKABLE OBSERVATIONS
	4M	K	21		NO REMARKABLE OBSERVATIONS
	5M	K	23		NO REMARKABLE OBSERVATIONS
	6F	K	23		NO REMARKABLE OBSERVATIONS
	7F	C	4		NO REMARKABLE OBSERVATIONS
	8F	K	21		NO REMARKABLE OBSERVATIONS
	9F	K	21		NO REMARKABLE OBSERVATIONS
	10F	K	21		NO REMARKABLE OBSERVATIONS
	11F	C	4	STOMACH	NO MILK IN STOMACH
	13F	S		LUNGS	FLOATATION TEST - STILLBORN
				STOMACH	NO MILK IN STOMACH

SEX CODES: M=Male, F=Female, U=Undetermined

PUP STATUS CODES: S-STILLBORN C-CULLED K-SCHEDULED SACRIFICE

APPENDIX CC - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 5 1000 MG/KG/DAY

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
5563	1U	Z	0	GROSS EXAM	CANNIBALIZED
	2M	S		GROSS EXAM	AUTOLYSIS
	3F	D	0	LUNGS	FLOATATION TEST - FOUND DEAD
				STOMACH	MILK IN STOMACH
	4F	S		GROSS EXAM	CANNIBALIZED
	5F	S		GROSS EXAM	CANNIBALIZED
	7M	D	2	STOMACH	NO MILK IN STOMACH
	8F	K	21		NO REMARKABLE OBSERVATIONS
	10F	K	23		NO REMARKABLE OBSERVATIONS
	11F	K	21		NO REMARKABLE OBSERVATIONS
	13F	D	0	STOMACH	NO MILK IN STOMACH
				LUNGS	FLOATATION TEST - FOUND DEAD
5564	1F	S		GROSS EXAM	AUTOLYSIS
	2M	K	23		NO REMARKABLE OBSERVATIONS
	3M	K	21		NO REMARKABLE OBSERVATIONS
	4M	K	21	GONADS	M UNDESCENDED TESTE(S); BILATERAL TISSUE SAVED
	5M	K	21		NO REMARKABLE OBSERVATIONS
	7M	C	4		NO REMARKABLE OBSERVATIONS
	8F	C	4		NO REMARKABLE OBSERVATIONS
	9F	C	4		NO REMARKABLE OBSERVATIONS
	10F	K	21		NO REMARKABLE OBSERVATIONS
	12F	K	21		NO REMARKABLE OBSERVATIONS
	13F	K	23		NO REMARKABLE OBSERVATIONS
	14F	K	21		NO REMARKABLE OBSERVATIONS
5565	1M	K	23		NO REMARKABLE OBSERVATIONS
	2M	K	21		NO REMARKABLE OBSERVATIONS
	3M	C	4		NO REMARKABLE OBSERVATIONS
	5M	C	4		NO REMARKABLE OBSERVATIONS
	6M	K	21		NO REMARKABLE OBSERVATIONS
	7M	C	4		NO REMARKABLE OBSERVATIONS
	8M	C	4		NO REMARKABLE OBSERVATIONS
	9M	K	21		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined

PUP STATUS CODES: S-STILLBORN D-DIED C-CULLED Z-CANNIBALIZED K-SCHEDULED SACRIFICE

APPENDIX CC - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 5 1000 MG/KG/DAY

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
5565	(CONTINUED)				
	10F	K	21		NO REMARKABLE OBSERVATIONS
	11F	K	21		NO REMARKABLE OBSERVATIONS
	12F	C	4		NO REMARKABLE OBSERVATIONS
	13F	K	23		NO REMARKABLE OBSERVATIONS
	14F	D	3	STOMACH	NO MILK IN STOMACH
	15F	K	21		NO REMARKABLE OBSERVATIONS
	16F	C	4		NO REMARKABLE OBSERVATIONS
5566	1M	C	4		NO REMARKABLE OBSERVATIONS
	4M	K	21		NO REMARKABLE OBSERVATIONS
	5M	C	4		NO REMARKABLE OBSERVATIONS
	6M	K	21		NO REMARKABLE OBSERVATIONS
	7M	K	23		NO REMARKABLE OBSERVATIONS
	8F	C	4		NO REMARKABLE OBSERVATIONS
	9F	C	4		NO REMARKABLE OBSERVATIONS
	10F	K	23		NO REMARKABLE OBSERVATIONS
	12F	K	21		NO REMARKABLE OBSERVATIONS
	13F	K	21		NO REMARKABLE OBSERVATIONS
	14F	K	21		NO REMARKABLE OBSERVATIONS
5567	1M	K	21		NO REMARKABLE OBSERVATIONS
	2M	K	21		NO REMARKABLE OBSERVATIONS
	3M	K	21		NO REMARKABLE OBSERVATIONS
	5M	C	4		NO REMARKABLE OBSERVATIONS
	6M	C	4		NO REMARKABLE OBSERVATIONS
	7M	C	4		NO REMARKABLE OBSERVATIONS
	8M	K	23		NO REMARKABLE OBSERVATIONS
	9F	K	21		NO REMARKABLE OBSERVATIONS
	10F	C	4		NO REMARKABLE OBSERVATIONS
	11F	C	4		NO REMARKABLE OBSERVATIONS
	12F	K	21		NO REMARKABLE OBSERVATIONS
	13F	K	23		NO REMARKABLE OBSERVATIONS
	14F	C	4		NO REMARKABLE OBSERVATIONS
	15F	K	21		NO REMARKABLE OBSERVATIONS

SEX CODES: M=Male, F=Female, U=Undetermined

PUP STATUS CODES: D-DIED C-CULLED K-SCHEDULED SACRIFICE

APPENDIX CC - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 5 1000 MG/KG/DAY

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
5568	1M	C	4		NO REMARKABLE OBSERVATIONS
	2M	K	21		NO REMARKABLE OBSERVATIONS
	3M	K	23		NO REMARKABLE OBSERVATIONS
	4M	K	21		NO REMARKABLE OBSERVATIONS
	6M	C	4		NO REMARKABLE OBSERVATIONS
	7M	K	21		NO REMARKABLE OBSERVATIONS
	8F	K	21		NO REMARKABLE OBSERVATIONS
	10F	K	23		NO REMARKABLE OBSERVATIONS
	12F	K	21		NO REMARKABLE OBSERVATIONS
	13F	K	21		NO REMARKABLE OBSERVATIONS
	14F	C	4		NO REMARKABLE OBSERVATIONS
5569	2M	K	21		NO REMARKABLE OBSERVATIONS
	3M	K	21		NO REMARKABLE OBSERVATIONS
	4M	C	4		NO REMARKABLE OBSERVATIONS
	6M	K	23		NO REMARKABLE OBSERVATIONS
	7M	C	4		NO REMARKABLE OBSERVATIONS
	8M	K	21		NO REMARKABLE OBSERVATIONS
	9F	K	21		NO REMARKABLE OBSERVATIONS
	11F	K	21		NO REMARKABLE OBSERVATIONS
	12F	K	21		NO REMARKABLE OBSERVATIONS
	13F	K	23		NO REMARKABLE OBSERVATIONS
5570	1M	D	0	LUNGS STOMACH	FLOATATION TEST - FOUND DEAD NO MILK IN STOMACH
	2M	S		GROSS EXAM	AUTOLYSIS
	3M	K	21		NO REMARKABLE OBSERVATIONS
	4M	K	21		NO REMARKABLE OBSERVATIONS
	5M	K	21	SKIN	SCAB LEFT CERVICAL AREA, RED, 1.0 X 1.0 CM TISSUE SAVED
	6M	K	23		NO REMARKABLE OBSERVATIONS
	8F	D	1	LUNGS STOMACH	FLOATATION TEST - FOUND DEAD MILK IN STOMACH
	9F	K	23		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined

PUP STATUS CODES: S-STILLBORN D-DIED C-CULLED K-SCHEDULED SACRIFICE

APPENDIX CC - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 5 1000 MG/KG/DAY

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
5570	(CONTINUED)				
	10F	K	21		NO REMARKABLE OBSERVATIONS
	11F	K	21		NO REMARKABLE OBSERVATIONS
5571	TLL	1M	S	GROSS EXAM	AUTOLYSIS
		4M	D	2 STOMACH	NO MILK IN STOMACH
		6M	D	1 LUNGS	FLOATATION TEST - FOUND DEAD
				STOMACH	NO MILK IN STOMACH
		8M	D	1 GROSS EXAM	AUTOLYSIS
		14F	Z	1 GROSS EXAM	CANNIBALIZED
				LUNGS	FLOATATION TEST - FOUND DEAD
		15F	D	1 GROSS EXAM	AUTOLYSIS
		16F	D	1 LUNGS	FLOATATION TEST - FOUND DEAD
				STOMACH	NO MILK IN STOMACH
5573		1M	D	1 LUNGS	FLOATATION TEST - FOUND DEAD
				STOMACH	NO MILK IN STOMACH
		2M	D	1 LUNGS	FLOATATION TEST - FOUND DEAD
				STOMACH	NO MILK IN STOMACH
		3M	D	1 LUNGS	FLOATATION TEST - FOUND DEAD
				STOMACH	NO MILK IN STOMACH
		4F	D	1 LUNGS	FLOATATION TEST - FOUND DEAD
				STOMACH	NO MILK IN STOMACH
		5F	D	1 LUNGS	FLOATATION TEST - FOUND DEAD
				STOMACH	NO MILK IN STOMACH
		6F	D	1 LUNGS	FLOATATION TEST - FOUND DEAD
				STOMACH	NO MILK IN STOMACH
		7M	D	5 GROSS EXAM	AUTOLYSIS
		8M	K	21	NO REMARKABLE OBSERVATIONS
		10M	K	21	NO REMARKABLE OBSERVATIONS
		11M	D	1 LUNGS	FLOATATION TEST - FOUND DEAD
				STOMACH	NO MILK IN STOMACH
		12M	K	21	NO REMARKABLE OBSERVATIONS
		13M	D	1 LUNGS	FLOATATION TEST - FOUND DEAD
				STOMACH	NO MILK IN STOMACH
		14M	K	28	NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F-Female, U=Undetermined

PUP STATUS CODES: S-STILLBORN D-DIED Z-CANNIBALIZED K-SCHEDULED SACRIFICE

TLL=TOTAL LITTER LOSS

APPENDIX CC - F1 GENERATION

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 5 1000 MG/KG/DAY

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
5573	(CONTINUED)				
	15F	D	1	LUNGS STOMACH	FLOATATION TEST - FOUND DEAD NO MILK IN STOMACH
5574	1F	D	0	LUNGS STOMACH	FLOATATION TEST - FOUND DEAD NO MILK IN STOMACH
	2M	D	0	LUNGS STOMACH	FLOATATION TEST - FOUND DEAD NO MILK IN STOMACH
	4M	K	23		NO REMARKABLE OBSERVATIONS
	6M	K	21		NO REMARKABLE OBSERVATIONS
	7F	K	23		NO REMARKABLE OBSERVATIONS

SEX CODES: M=Male, F=Female, U=Undetermined

PUP STATUS CODES: D-DIED K-SCHEDULED SACRIFICE

APPENDIX DD - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL NECROPSY OBSERVATIONS

GROUP 1 0 MG/KG/DAY

ANIMAL#	ORGAN	OBSERVATION
1075	KIDNEY KIDNEY KIDNEY	DILATED RENAL PELVIS; EXTREME; RIGHT ENLARGED KIDNEY; EXTREME; RIGHT SMALL KIDNEY; EXTREME LEFT, 0.5 CM, NOT DEVELOPED
1076		NO REMARKABLE OBSERVATIONS
1077		NO REMARKABLE OBSERVATIONS
1078		NO REMARKABLE OBSERVATIONS
1079		NO REMARKABLE OBSERVATIONS
1080		NO REMARKABLE OBSERVATIONS
1081		NO REMARKABLE OBSERVATIONS
1082		NO REMARKABLE OBSERVATIONS
1083		NO REMARKABLE OBSERVATIONS
1084		NO REMARKABLE OBSERVATIONS
1085		NO REMARKABLE OBSERVATIONS

6-FEB-2004 11:28

Huntingdon Life Sciences 03-4254P

PAGE 520

APPENDIX DD - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

GROUP 2 64 MG/KG/DAY		INDIVIDUAL NECROPSY OBSERVATIONS
ANIMAL#	ORGAN	OBSERVATION
2075		NO REMARKABLE OBSERVATIONS
2076		NO REMARKABLE OBSERVATIONS
2077		NO REMARKABLE OBSERVATIONS
2078		NO REMARKABLE OBSERVATIONS
2079		NO REMARKABLE OBSERVATIONS
2080		NO REMARKABLE OBSERVATIONS
2081		NO REMARKABLE OBSERVATIONS
2082		NO REMARKABLE OBSERVATIONS
2083		NO REMARKABLE OBSERVATIONS
2084		NO REMARKABLE OBSERVATIONS
2085		NO REMARKABLE OBSERVATIONS

6-FEB-2004 11:28

Huntingdon Life Sciences 03-4254P

PAGE 521

APPENDIX DD - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL NECROPSY OBSERVATIONS

GROUP 3 160 MG/KG/DAY

ANIMAL#	ORGAN	OBSERVATION
3075		NO REMARKABLE OBSERVATIONS
3076		NO REMARKABLE OBSERVATIONS
3077		NO REMARKABLE OBSERVATIONS
3078		NO REMARKABLE OBSERVATIONS
3079		NO REMARKABLE OBSERVATIONS
3080		NO REMARKABLE OBSERVATIONS
3081		NO REMARKABLE OBSERVATIONS
3082		NO REMARKABLE OBSERVATIONS
3083		NO REMARKABLE OBSERVATIONS
3084		NO REMARKABLE OBSERVATIONS
3085		NO REMARKABLE OBSERVATIONS

6-FEB-2004 11:28

Huntingdon Life Sciences 03-4254P

PAGE 522

APPENDIX DD - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL NECROPSY OBSERVATIONS

GROUP 4 400 MG/KG/DAY

ANIMAL#	ORGAN	OBSERVATION
4075		NO REMARKABLE OBSERVATIONS
4076		NO REMARKABLE OBSERVATIONS
4077		NO REMARKABLE OBSERVATIONS
4078		NO REMARKABLE OBSERVATIONS
4079		NO REMARKABLE OBSERVATIONS
4080		NO REMARKABLE OBSERVATIONS
4081		NO REMARKABLE OBSERVATIONS
4082		NO REMARKABLE OBSERVATIONS
4083		NO REMARKABLE OBSERVATIONS
4084		NO REMARKABLE OBSERVATIONS
4085		NO REMARKABLE OBSERVATIONS
4086		NO REMARKABLE OBSERVATIONS

6-FEB-2004 11:28

Huntingdon Life Sciences 03-4254P

PAGE 523

APPENDIX DD - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL NECROPSY OBSERVATIONS

GROUP 5 1000 MG/KG/DAY

ANIMAL#	ORGAN	OBSERVATION
5075		NO REMARKABLE OBSERVATIONS
5076		NO REMARKABLE OBSERVATIONS
5077		NO REMARKABLE OBSERVATIONS
5078		NO REMARKABLE OBSERVATIONS
5079		NO REMARKABLE OBSERVATIONS
5080		NO REMARKABLE OBSERVATIONS
5081		NO REMARKABLE OBSERVATIONS
5082		NO REMARKABLE OBSERVATIONS
5083		NO REMARKABLE OBSERVATIONS
5084		NO REMARKABLE OBSERVATIONS

6-FEB-2004 11:28

Huntingdon Life Sciences 03-4254P

PAGE 524

APPENDIX DD - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL NECROPSY OBSERVATIONS

GROUP 1 0 MG/KG/DAY

ANIMAL#	ORGAN	OBSERVATION
1575		NO REMARKABLE OBSERVATIONS
1576		NO REMARKABLE OBSERVATIONS
1577		NO REMARKABLE OBSERVATIONS
1578		NO REMARKABLE OBSERVATIONS
1579		NO REMARKABLE OBSERVATIONS
1580		NO REMARKABLE OBSERVATIONS
1581		NO REMARKABLE OBSERVATIONS
1582		NO REMARKABLE OBSERVATIONS
1583		NO REMARKABLE OBSERVATIONS
1584		NO REMARKABLE OBSERVATIONS
1585		NO REMARKABLE OBSERVATIONS

APPENDIX DD - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL NECROPSY OBSERVATIONS

GROUP 2 64 MG/KG/DAY

ANIMAL#	ORGAN	OBSERVATION
2575		NO REMARKABLE OBSERVATIONS
2576		NO REMARKABLE OBSERVATIONS
2577	KIDNEY	CYSTIC KIDNEY; LEFT CORTEX, 0.1 CM IN DIAMETER, CLEAR, MULTIPLE
2578		NO REMARKABLE OBSERVATIONS
2579		NO REMARKABLE OBSERVATIONS
2580		NO REMARKABLE OBSERVATIONS
2581		NO REMARKABLE OBSERVATIONS
2582		NO REMARKABLE OBSERVATIONS
2583		NO REMARKABLE OBSERVATIONS
2584		NO REMARKABLE OBSERVATIONS
2585	KIDNEY	DILATED RENAL PELVIS; MODERATE; RIGHT

6-FEB-2004 11:28

Huntingdon Life Sciences 03-4254P

PAGE 526

APPENDIX DD - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL NECROPSY OBSERVATIONS

GROUP 3 160 MG/KG/DAY

ANIMAL#	ORGAN	OBSERVATION
3575		NO REMARKABLE OBSERVATIONS
3576		NO REMARKABLE OBSERVATIONS
3577		NO REMARKABLE OBSERVATIONS
3578		NO REMARKABLE OBSERVATIONS
3579		NO REMARKABLE OBSERVATIONS
3580		NO REMARKABLE OBSERVATIONS
3581		NO REMARKABLE OBSERVATIONS
3582		NO REMARKABLE OBSERVATIONS
3583		NO REMARKABLE OBSERVATIONS
3584		NO REMARKABLE OBSERVATIONS
3585		NO REMARKABLE OBSERVATIONS
3586		NO REMARKABLE OBSERVATIONS

6-FEB-2004 11:28

Huntingdon Life Sciences 03-4254P

PAGE 527

APPENDIX DD - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL NECROPSY OBSERVATIONS

GROUP 4 400 MG/KG/DAY

ANIMAL#	ORGAN	OBSERVATION
4575		NO REMARKABLE OBSERVATIONS
4576		NO REMARKABLE OBSERVATIONS
4577		NO REMARKABLE OBSERVATIONS
4578		NO REMARKABLE OBSERVATIONS
4579		NO REMARKABLE OBSERVATIONS
4580		NO REMARKABLE OBSERVATIONS
4581		NO REMARKABLE OBSERVATIONS
4582		NO REMARKABLE OBSERVATIONS
4583		NO REMARKABLE OBSERVATIONS
4584		NO REMARKABLE OBSERVATIONS
4585		NO REMARKABLE OBSERVATIONS
4586		NO REMARKABLE OBSERVATIONS

APPENDIX DD - F1 TREATED ANIMALS

TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
IN RATS

INDIVIDUAL NECROPSY OBSERVATIONS

GROUP 5 1000 MG/KG/DAY

ANIMAL#	ORGAN	OBSERVATION
5575		NO REMARKABLE OBSERVATIONS
5576		NO REMARKABLE OBSERVATIONS
5577		NO REMARKABLE OBSERVATIONS
5578		NO REMARKABLE OBSERVATIONS
5579		NO REMARKABLE OBSERVATIONS
5580		NO REMARKABLE OBSERVATIONS
5581		NO REMARKABLE OBSERVATIONS
5582		NO REMARKABLE OBSERVATIONS
5583	KIDNEY	DILATED RENAL PELVIS; MODERATE; RIGHT
5584		NO REMARKABLE OBSERVATIONS

	Sperm Analysis Report (Pathology Associates International)	Appendix EE
--	---	-------------

SPERM ANALYSIS REPORT

FOR

TBA:
REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

HLS STUDY NUMBER: 03-4254

PREPARED FOR

HUNTINGDON LIFE SCIENCES (HLS)
100 METTLERS ROAD
P.O. Box 2360
EAST MILLSTONE, NJ 08875-2360

PREPARED BY

PATHOLOGY ASSOCIATES (PAI)
A DIVISION OF CHARLES RIVER LABORATORIES, INC.

TABLE OF CONTENTS

<u>Section</u>	<u>Page No.</u>
I. QUALITY ASSURANCE STATEMENT	4
II. MATERIALS AND METHODS	5
A. Sample Collection	5
B. Sperm Motility Evaluation	5
C. Total Sperm Count Determination.....	6
D. Sperm Morphology Evaluation	6
E. Statistical Analyses	6
F. GLP Compliance Statement	6
G. Material Archiving	7
III. RESULTS	7
A. Sperm Motility	7
B. Total Sperm Count	7
C. Sperm Morphology	8
IV. DISCUSSION AND CONCLUSIONS	8
V. REFERENCES	8

INDEX OF TABLES AND APPENDICES

<u>Table</u>	<u>Page No.</u>
--------------	-----------------

1. Summary of Sperm Analysis Parameters	9
---	---

<u>Appendix</u>	<u>Page No.</u>
-----------------	-----------------

A. Individual Sperm Motility and Sperm Count Data	10
B. Individual Sperm Morphology Data	11

Sperm Analysis Report

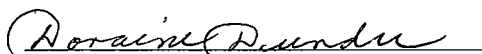
Reproduction/Developmental Toxicity Screening Test

Huntingdon Life Sciences Study Number: 03-4254

QUALITY ASSURANCE STATEMENT

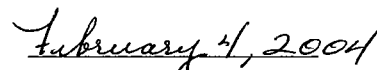
This sperm analysis project has been inspected and audited by the PAI Quality Assurance Unit (QAU) as required by the Good Laboratory Practice (GLP) regulations promulgated by the U.S. Environmental Protection Agency (EPA) and the Organization for Economic Cooperation and Development (OECD). The sperm analysis report is an accurate reflection of the recorded data. The following table is a record of the inspections/audits performed and reported by the QAU.

<u>Date of Inspection</u>	<u>Phase Inspected</u>	<u>Date Findings Reported to Reproductive Toxicologist/PAI Management*</u>	<u>Date Findings Reported to Study Director/Study Director Management</u>
09/03/03	Sperm Count	09/03/03	09/03/03
09/08/03	Individual Animal Data	09/08/03	09/08/03
09/08/03	Draft Sperm Analysis Report	09/08/03	09/08/03
10/23/03	2 nd Draft Sperm Analysis Report	10/23/03	10/23/03
02/04/04	Final Sperm Analysis Report	02/04/04	02/04/04



Doraine Dundee

Quality Assurance Specialist


Date

*And the Principal Investigator/Principal Investigator Management

TBA:
Reproduction/Developmental Toxicity Screening Test in Rats

II. MATERIALS AND METHODS

A. Sample Collection

After at least 9 weeks of treatment, all F₀ male rats were euthanized by exposure to carbon dioxide. For all animals, the abdominal cavity was opened and the reproductive organs exposed. For motility assessment, the right vas deferens was dissected away from the testis and immediately placed in a petri dish containing 10 ml of a solution consisting of 1% Bovine Serum Albumin dissolved in Phosphate Buffered Saline. The solution was prewarmed to a temperature of approximately 38°C. A minimum 3-minute period was allowed for the sperm to swim out.

For total sperm and spermatid count assessment, the right epididymis and right testis, respectively, were then removed and placed on dry ice. The frozen epididymides and testes were then transferred to Pathology Associates, A Division of Charles River Laboratories, Inc. (formerly known as Pathology Associates International until January 8, 2001), Frederick, MD. and stored frozen at -70°C or below until evaluation for caudal epididymal sperm count and homogenization-resistant testicular spermatid count.

Only the control and high dose group animals were examined for percent motility, total epididymal sperm count, testicular spermatid count and sperm morphology. Samples were collected and evaluated using the Hamilton Thorne Integrated Visual Optical System (IVOS) sperm analyzer, software version 12.1c.

B. Sperm Motility Evaluation

Following the swim out period, a sperm sample was obtained using a 100 µm deep cannula. The cannula was immediately loaded into the prewarmed stage of the Hamilton Thorne IVOS automated sperm analyzer. The analyzer automatically selected five fields and each motion image was digitally saved and permanently stored on optical media. The images were subsequently analyzed and the percent motility determined for each animal.

C. Total Sperm Count Determination

Each frozen epididymis was removed from the freezer, thawed and the caudal section was trimmed and weighed. Each frozen testis was removed from the freezer, thawed, the tunica removed and the testicular parenchyma weighed. The cauda epididymis and testicular parenchyma were homogenized in deionized water and the suspensions were transferred to plastic test tubes and vortexed. A 100 μ l sample was transferred to a violet reaction vial containing a Hoechst dye (H33342) which uniquely stains the head of the sperm. A sample of the stained sperm was placed into a 20 μ m deep Cell-Vu glass slide which was loaded into the analyzer. Twenty fields were automatically selected by the analyzer for each animal and the number of cauda epididymal sperm and homogenization-resistant spermatids determined. The counts reported were adjusted for caudal epididymal or testicular weight.

D. Sperm Morphology Evaluation

Two Eosin stained slides were prepared for each animal from the caudal epididymis total count preparation. The slides were evaluated and a minimum of 200 sperm cells/animal was examined for morphological development.

E. Statistical Analyses

The means and standard deviations for the sperm motility, caudal epididymal sperm count, testicular homogenization-resistant spermatid count and sperm morphology data were calculated and compared across groups using the Kruskal-Wallis nonparametric ANOVA test. Statistical analyses were performed using an IBMTM compatible computer with SAS computer programs (SAS/STAT User's Guide, 1989).

F. GLP Compliance Statement

The portion of this study performed by PAI was conducted in compliance with EPA Good Laboratory Practices as set forth in 40 CFR Part 792 (TSCA) and Organization for Economic Cooperation and Development (OECD) Good Laboratory Practices as set forth in ENV/MC/CHEM(98)17.

G. Material Archiving

The optical media used for permanent storage of the sperm motility images, raw data printouts from the sperm motility, epididymal sperm and testicular spermatid count determinations, sperm morphology slides, remaining frozen epididymal and testicular tissue from the low, lower mid and upper mid dose groups, as well as any supporting documentation, will be returned to HLS for archiving.

III. RESULTS

A. Sperm Motility

Table 1 (Summary Data)
Appendix A (Individual Data)

A slight, though statistically significant, decrease in the percent motility was observed in the high-dose group. Group mean values were 94% for the control and 91% for the high-dose group. The mean percent motility in the high-dose group remained above 90%, therefore this minor reduction was not considered treatment-related.

B. Total Sperm Count

Table 1 (Summary Data)
Appendix A (Individual Data)

No apparent treatment-related effects were observed in the epididymal sperm or testicular spermatid counts. The number of sperm per gram of caudal epididymis was comparable between the dose groups and was 747.4 and 751.6 million sperm/gram of caudal epididymal tissue for the control and high-dose group, respectively. The number of spermatids per gram of testis was 106.8 (million) for the control and 110.2 (million) for the high-dose group.

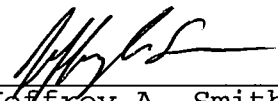
C. Sperm Morphology

Table 1 (Summary Data)
Appendix B (Individual Data)

A low incidence of head abnormalities was observed for animals in the control and high-dose groups. Group mean values were 0.9 and 1.3 percent abnormal sperm. No treatment related differences were observed.

IV. DISCUSSION AND CONCLUSIONS

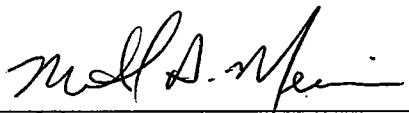
A statistically significant incidental decrease in the percent motility was observed in the 1000 mg/kg/day dose group. A decrease of this magnitude is not considered treatment-related or biologically meaningful. Other sperm analysis parameters, including the mean epididymal sperm count, testicular spermatid count and sperm morphology were not affected by treatment with TBA at a dose level of 1000 mg/kg/day. No biologically meaningful differences were observed between the study groups for any sperm analysis parameter.



Jeffrey A. Smith, M.S.
Senior Staff Scientist
Pathology Associates
A Division of Charles River Laboratories, Inc.

2/4/04

Date



Michael D. Mercieca, B.S.
Principal Investigator
Pathology Associates
A Division of Charles River Laboratories, Inc.

2/4/04

Date

V. REFERENCES

SAS/STAT User's Guide, 1989a. SAS Institute Inc., Version 6, Fourth Edition, Cary, NC:SAS Institute Inc., 1989. Vol. 1, p. 209-244. Vol. 2 p. 1195-1210.

HLS STUDY NO.: 03-4254

TABLE 1

TBA:
REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

SUMMARY OF SPERM ANALYSIS PARAMETERS

Group:		1	5
Dose Level:	TBA (mg/kg/day)	0	1000
<hr/>			
MOTILITY (%)			
Mean		94	91*
SD		6	5
N		12	12
EPIDIDYMAL SPERM COUNT			
(MILLION SPERM/GRAM)			
Mean		747.4	751.6
SD		157.1	107.5
N		12	12
TESTICULAR SPERMATID COUNT			
(MILLION SPERM/GRAM)			
Mean		106.8	110.2
SD		16.9	14.2
N		12	12
SPERM MORPHOLOGY ^a			
(% ABNORMAL)			
Mean		0.9	1.3
SD		0.8	0.8
N		12	12

^aMEAN AND STANDARD DEVIATIONS WERE CALCULATED USING THE TOTAL NUMBER OF ABNORMAL SPERM AS A PERCENTAGE OF THE NUMBER OF SPERM EXAMINED.

*SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP ($p < 0.05$).

HLS STUDY NO.: 03-4254

APPENDIX A

TBA:
REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL SPERM MOTILITY AND SPERM COUNT DATA

Group 1: 0 mg/kg/day (TBA)

Animal No.	Motility (%)	S P E R M C O U N T	
		Caudal Epididymal (million/gram)	Homogenization Resistant Testicular Spermatid
1063	98	812.4	124.3
1064	96	814.1	127.6
1065	95	452.0	104.6
1066	98	698.5	90.0
1067	96	731.9	119.5
1068	98	672.7	102.1
1069	85	627.4	126.9
1070	98	736.7	108.9
1071	91	603.3	87.5
1072	99	852.4	78.7
1073	80	914.9	119.2
1074	94	1052.4	92.2

Group 5: 1000 mg/kg/day (TBA)

Animal No.	Motility (%)	S P E R M C O U N T	
		Caudal Epididymal (million/gram)	Homogenization Resistant Testicular Spermatid
5063	90	596.9	133.8
5064	94	937.2	115.1
5065	91	921.0	90.4
5066	96	693.2	93.3
5067	93	647.5	113.4
5068	90	787.7	89.5
5069	84	818.5	119.3
5070	93	731.9	119.9
5071	97	795.4	109.7
5072	93	770.7	99.1
5073	88	644.1	123.8
5074	79	674.9	115.1

HLS STUDY NO.: 03-4254

APPENDIX B

TBA:
REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL SPERM MORPHOLOGY DATA

Group 1: 0 mg/kg/day (TBA)

Animal No.	Normal	-----H e a d-----				-----T a i l-----			
		Amorphous	Small	Enlarged	Double	Coiled	Bent	Double	Other
1063	200	0	0	0	0	0	0	0	0
1064	198	2	0	0	0	0	0	0	0
1065	197	3	0	0	0	0	0	0	0
1066	199	1	0	0	0	0	0	0	0
1067	200	0	0	0	0	0	0	0	0
1068	198	1	1	0	0	0	0	0	0
1069	199	1	0	0	0	0	0	0	0
1070	196	4	0	0	0	0	0	0	0
1071	198	1	1	0	0	0	0	0	0
1072	200	0	0	0	0	0	0	0	0
1073	195	5	0	0	0	0	0	0	0
1074	198	2	0	0	0	0	0	0	0

HLS STUDY NO.: 03-4254

APPENDIX B

TBA:
REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS

INDIVIDUAL SPERM MORPHOLOGY DATA

Group 5: 1000 mg/kg/day (TBA)

Animal No.	Normal	-----H e a d-----				-----T a i l-----			
		Amorphous	Small	Enlarged	Double	Coiled	Bent	Double	Other
5063	198	2	0	0	0	0	0	0	0
5064	197	3	0	0	0	0	0	0	0
5065	199	1	0	0	0	0	0	0	0
5066	196	4	0	0	0	0	0	0	0
5067	200	0	0	0	0	0	0	0	0
5068	197	3	0	0	0	0	0	0	0
5069	196	4	0	0	0	0	0	0	0
5070	199	1	0	0	0	0	0	0	0
5071	196	4	0	0	0	0	0	0	0
5072	199	1	0	0	0	0	0	0	0
5073	196	4	0	0	0	0	0	0	0
5074	195	5	0	0	0	0	0	0	0

Huntingdon Life Sciences Historical Control Data
For Sperm Motility

Appendix EE (b)

Sperm Motility (Computer-Assisted Semen Analysis derived):

Laboratory Background Control Data

Period: Male Terminations Oct 2001 to Dec 2002

Study	Control Group Mean Sperm Motility \pm SD
1	91 \pm 9
2	92 \pm 9
3	92 \pm 6
4	91 \pm 19
5	96 \pm 3
6	93 \pm 11
7	90 \pm 20
8	95 \pm 3
9	89 \pm 6

	Certificate of Analysis for the Test Article	Appendix FF
--	--	-------------

Certificate Of Analysis

Certificate of Analysis Contact:

HUNTINGTON LIFE SCIENCES
METTLERS ROAD
EAST MILLSTONE NJ 08875

Ship-To Address:

HUNTINGTON LIFE SCIENCES
METTLERS ROAD
EAST MILLSTONE NJ 08875
USA

Lyondell Material : 499248 TEBOL ® 99
Chemical Description : High Purity Tertiary Butyl Alcohol
Batch Number : HL30408005
Estimated Quantity : 7 LBS

Customer Order No. : HPV-HUNTINGDON
Customer Number : SAMPLES
Date Shipped : April 07, 2003
Lyondell Order No. : 727132 000010
Delivery Item No. : 80905894 000010

Test Description	Test Result	Specifications		Unit of Measure
		Minimum	Maximum	
Miscellaneous Text	3 GALLON SAMPLE TO ABC LAB			
TBA	99.58	99.30		weight %
Water	0.0200		0.1500	weight %
Distillation IBP @760 mmHg	82.4	81.5		degrees C
Distillation DP @760 mmHg	82.7		83.0	degrees C
Acidity (as acetic acid)	0.0000		0.0030	weight %
APHA Color	4		10	APHA Color
Freezing point	25.0	24.0		degrees C
Non-volatiles	0.0005		0.0010	g/100 ml

APPROVED BY:


Ed Campbell

Print Date: June 16, 2003

MXSHARO

This information is available 24 hours a day at

www.CustomerXPRESS.com

Questions ? Call Customer Service: 888-777-0232

This Certificate of Analysis contains the most current information available as of the print date.

This document shall not be reproduced except in full, without the written approval of the issuer.

	Testing Facility Personnel	Appendix GG
--	----------------------------	-------------

TITLE/DEPARTMENT	NAME/DEGREE
SENIOR VICE PRESIDENT, SAFETY ASSESSMENT	Sylvie J. Gosselin, D.V.M., Ph.D., Diplomate A.C.V.P.
DIRECTOR, ANALYTICAL SERVICES	Barbara A. Litzenberger, B.S., M.T. (ASCP)
DIRECTOR, TOXICOLOGY OPERATIONS	Ian Vanterpool, F.I.A.T.
DIRECTOR, QUALITY ASSURANCE	Nicki S. Iacono, B.S.
STUDY DIRECTOR, DIRECTOR, REPRODUCTIVE TOXICOLOGY	Keith P. Hazelden, BSc, CBiol, MIBiol
PATHOLOGIST	Dianne Creasy, Ph.D., DipRCPath (Tox), FRCPath.
VETERINARIAN	Teresa S. Kuszniir, V.M.D.
REPORT PRODUCTION	Janet E. Scimone, B.A.
MANAGER/SUPERVISOR	
Reproductive Toxicology	Robert Faust, B.S.
Fetal Pathology	G. Elizabeth Baxter, B.S.
Analytical Services	Kay Saladdin, B.S.
Pharmacy	Michael S. McCarthy
Histology	Janet Kusisto, B.S., H.T. (ASCP)

PROTOCOL

TBA

REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS (Modified OECD 421 Design)

CONFIDENTIAL

HLS Study No.:	03-4254
Protocol Version:	Final
Date:	23 May 2003

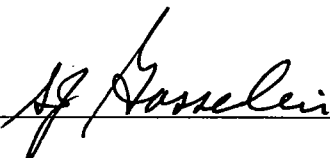
PROTOCOL SIGNATURES/PREFACE

(Confidential Information - to be distributed on a need-to-know basis)

Study Title: TBA: Reproduction/Developmental Toxicity Screening Test
in Rats

HLS Study No.: 03-4254

This is the Final Protocol. It is approved by:

Keith P Hazelden, BSc, CBiol, MIBiol
Study Director
Huntingdon Life Sciences23 May 03
DateSylvie J Gosselin, DVM, PhD, ACVP
Facility Management
Huntingdon Life Sciences28 May 2003
DateRobert J Fensterheim
Propylene Carbonate/t-Butyl Alcohol
HPV Committee6 June 2003
Date

CONFIDENTIAL STUDY SPECIFIC INFORMATION

Sponsor: Propylene Carbonate/t-Butyl Alcohol HPV Committee
1250 Connecticut Avenue NW, Suite 700
Washington DC 20036

Study Monitor: George Cruzan, PhD, DABT
ToxWorks
1153 Roadstown Road
Bridgeton, NJ 08302
Tel: 856 453 3478
Fax: 856 453 3479
Email: ToxWorks@aol.com

Study Director: Keith P Hazelden, BSc, CBiol, MIBiol
Huntingdon Life Sciences
PO Box 2360
East Millstone, NJ 08875-2360
Tel: 723 873 2550, Extn 2590
Fax: 732 873 3992
Email: hazeldek@princeton.huntingdon.com

Formulation concentration verification
(Principal Investigator): Kay A Saladdin
Chemistry Department
Huntingdon Life Sciences
PO Box 2360
East Millstone, NJ 08875-2360
Tel: 732 873 2550, Extn 6084
Fax: 732 873 3992
Email: saladdik@princeton.huntingdon.com

Seminology
(Principal Investigator): Michael D Mercieca, BS
Pathology Associates International
15 Worman's Mill Court, Suite 1
Frederick, MD 21701
Tel: 301 663 1644
Fax: 301 682 8387
Email: mmercieca@criver.com

Additional personnel will be documented in the project file and presented in the final report.

TBA:

REPRODUCTION/DEVELOPMENTAL TOXICITY

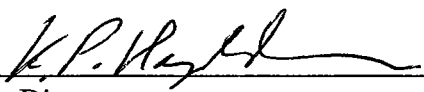
SCREENING TEST

(Modified OECD 421 design)

HLS Study No: 03-4254

Number of pages for general distribution: 26

This working document is approved for circulation and use:


Study Director

23 May 08
Date

Testing Facility

Materials/Courier delivery:

Huntingdon Life Sciences
Princeton Research Center
100 Mettlers Road
Somerset
NJ 08873
USA

USPS mail:

Huntingdon Life Sciences
Princeton Research Center
PO Box 2360
East Millstone
NJ 08875-2360
USA

All procedures to be performed at the above site.

TABLE OF CONTENTS

1. INTRODUCTION.....	4
2. STUDY PERSONNEL.....	4
3. PROPOSED STUDY DATES.....	5
4. EXPERIMENTAL DESIGN.....	6
4.1. STUDY SUMMARY	6
4.2. JUSTIFICATION FOR TEST SYSTEM SELECTION.....	7
4.3. JUSTIFICATION FOR ROUTE, DURATION AND FREQUENCY	7
4.4. JUSTIFICATION FOR NUMBER OF ANIMALS	7
4.5. JUSTIFICATION FOR DOSE LEVEL SELECTION	7
5. TEST AND CONTROL ARTICLES.....	8
5.1. TEST ARTICLE: TERTIARY BUTANOL (TBA).....	8
5.2. ARCHIVAL SAMPLES.....	9
5.3. UNUSED TEST ARTICLE.....	9
5.4. CONTROL ARTICLE (DOSING VEHICLE).....	9
5.5. PREPARATION OF DOSING FORMULATIONS.....	9
5.6. UNUSED DOSING FORMULATION	9
5.7. ANALYSIS OF DOSING FORMULATIONS	9
6. TEST ANIMALS	10
6.1. SPECIES AND STRAIN.....	10
6.2. SUPPLIER.....	10
6.3. ANIMAL REQUIREMENTS/SPECIFICATIONS	10
6.4. ANIMAL HUSBANDRY.....	11
6.5. ACCLIMATION PERIOD	12
6.6. ANIMAL ASSIGNMENT.....	12
6.7. ANIMAL IDENTIFICATION.....	13
6.8. MATING PROCEDURE.....	13
7. TEST ARTICLE ADMINISTRATION.....	13
7.1. ROUTE OF ADMINISTRATION	13
7.2. FREQUENCY AND DURATION OF ADMINISTRATION	13
7.3. ADMINISTRATION OF TEST ARTICLE	13
8. IN-LIFE EXPERIMENTAL OBSERVATIONS.....	14
8.1. CLINICAL OBSERVATIONS.....	14
8.2. BODY WEIGHTS	14
8.3. FEED CONSUMPTION	15
8.4. PARTURITION AND LACTATION	15
8.5. F ₁ PUP EVALUATIONS.....	16

8.6.	SELECTION OF F ₁ ANIMALS	16
9.	TERMINATION	16
9.1.	TERMINATION SCHEDULE	16
9.2.	METHODS OF EUTHANASIA	17
10.	TERMINAL OBSERVATIONS	17
10.1.	F ₀ ANIMALS	17
10.2.	F ₁ OFFSPRING: NON-SELECTED WEANLINGS (PND 21), AND DIRECTLY TREATED (PND 28)	19
10.3.	F ₁ PUPS: CULLED ON PND 4	19
10.4.	F ₁ PUPS: DECEDENT PRIOR TO WEANING	20
11.	PRESERVATION OF RECORDS AND SPECIMENS	20
12.	STATISTICAL EVALUATIONS	20
12.1.	CONTINUOUS DATA	20
12.2.	INCIDENCE DATA	22
13.	REPORTING	22
13.1.	STATUS REPORTS	22
13.2.	FINAL REPORT	23
14.	REGULATORY REFERENCES	24
14.1.	TEST GUIDELINE	24
14.2.	GOOD LABORATORY PRACTICES	24
14.3.	ANIMAL WELFARE ACT COMPLIANCE	25
14.4.	INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) ...	25
15.	QUALITY ASSURANCE MONITORING	26
16.	ALTERATION OF DESIGN	26

1. INTRODUCTION

This study is designed to provide limited information on possible effects of tertiary butanol, a chemical intermediate, on reproduction and development in rats. It will not provide complete information on all aspects, but should permit detection of effects on gonadal function, mating behavior, conception, development of the conceptus, parturition, pup survival and growth to weaning at post-natal day (PND) 21. Information will also be generated on the outcome of short-term direct exposure (dosing) of offspring immediately after weaning.

2. STUDY PERSONNEL

Study Director

Keith P Hazelden, BSc, CBiol, MIBiol
Tel.: 732-873-2550 x 2590
Fax: 732-873-3992

Alternate Contact

Edward R Frizell, MD, PhD
Tel.: 732-873-2550 x 2598
Fax: 732-873-3992

Additional personnel will be documented in the project file and presented in the final report.

3. PROPOSED STUDY DATES

Study Initiation Date:	Date Study Director Signs Protocol
Receipt of Test Animals:	3 June 2003
Initiation of Dosing:	17 June 2003
Initiation of Mating (pairing for up to 2 weeks):	15 July 2003
Parturition from:	6 August 2003
F ₀ male terminations:	20-22 August 2003
Weaning, F ₀ female and excess F ₁ terminations from:	27 August 2003
F ₁ (directly treated) terminations from:	3 September 2003
Submission of Draft Final Report:	19 December 2003
Study Completion Date:	Date final report is signed by Study Director

4. EXPERIMENTAL DESIGN**4.1. STUDY SUMMARY**

Group	Group Designation	Dose Levels (mg/kg/day)	Number of F ₀ Animals		Number of F ₁ Animals	
			Males ^a	Females ^b	Males ^c	Females ^c
1	Control	0	12	12	12	12
2	Low	64	12	12	12	12
3	Lower Mid	160	12	12	12	12
4	Upper Mid	400	12	12	12	12
5	High	1000	12	12	12	12

Dose volume: 5 ml/kg body weight, determined by the most recently recorded body weight.

- ^a Males will be dosed once daily, seven days/week for 4 weeks prior to pairing for mating. Dosing will continue during the mating and post-mating periods until sacrifice for necropsy and histopathology after an overall 9 weeks of treatment.
- ^b Females will be dosed once daily, seven days/week for 4 weeks prior to pairing for mating. Dosing will continue during mating, gestation and lactation until sacrifice for necropsy on post-natal day (PND) 21. Females without detected evidence of mating and/or that do not produce a litter will continue to be dosed for up to 24 days following completion of the mating period, prior to sacrifice and necropsy. F₁ offspring will not be treated directly prior to weaning and those not selected for post-weaning treatment will be sacrificed for necropsy on PND 21.
- ^c Weanlings, 1 male and 1 female from each available litter, will be dosed once daily on PND 21-27, then sacrificed for necropsy on PND 28.

The mating period will be for up to 2 weeks, one male to one female, continuously paired until evidence of mating is detected.

4.2. JUSTIFICATION FOR TEST SYSTEM SELECTION

The rat is a rodent animal model acceptable under OECD testing guidelines for reproductive toxicity studies. In addition, historical data are available in the Testing Facility with this strain of rat.

4.3. JUSTIFICATION FOR ROUTE, DURATION AND FREQUENCY

Oral ingestion is a possible route of human exposure to this test article, and once daily dosing by gavage is intended to achieve an adequate regime of continuous systemic exposure. Males are to be treated for at least 9 weeks overall, to ensure exposure of the entire process of spermatogenesis. A pre-mating treatment period of 4 weeks followed by a mating trial and detailed histopathological examination of the testes and epididymides is considered sufficient to enable detection of the majority of effects on spermatogenesis and male fertility. Females will be treated for the same 4-week pre-mating period as the males, permitting direct comparison of the gross clinical aspects of any toxicity over that period. Treatment of females will continue through to termination at weaning of their litter at post-natal day (PND) 21. This will ensure exposure of the female reproductive process from ovulation through conception, implantation, gestation, parturition and lactation. Selected offspring will be treated directly for one week after weaning, in order to establish whether or not weanlings will adequately tolerate the dose levels being applied to the adults in this study.

No adverse effects on the sex organs of rats or mice were seen in the subchronic or chronic toxicity studies on t-butanol (TBA) conducted by the National Toxicology Program. In developmental toxicity studies, however, reduced fetal body weight and altered post-natal development were suggested. No studies of the effects of TBA on general reproduction have been conducted and therefore, the present screening study is being undertaken.

4.4. JUSTIFICATION FOR NUMBER OF ANIMALS

The number of animals in this study is considered the minimum necessary to allow for meaningful interpretation of the data, as required by OECD guidelines. Ten pregnancies per group are considered adequate numbers for screening for developmental toxicities and provide the necessary degree of consistency between studies. The group size of 12 used in this study, with recent pregnancy rates of 80-90%, should provide the necessary numbers for evaluation.

4.5. JUSTIFICATION FOR DOSE LEVEL SELECTION

Previous studies performed under the National Toxicology Program included a 13-week toxicity study in rats and a 2-year study in rats, both by administration in the drinking water at levels of 2.5 to 40 mg/ml (13-week study) and 1.25 to 10 mg/ml (2-year study). The 40 mg/ml dosage proved lethal in the majority of animals in the 13-week study and final body weight of males at 10 and 20 mg/ml

was 12% and 17% less than Control. Liver and kidney weights, and the incidence of mineralization in the kidney, were increased at all dosages and there was increased incidence/severity of nephropathy. There was also increased activity of sorbitol dehydrogenase and alanine aminotransferase, with decreased urine volume and increased urine specific gravity. Hyperplasia and inflammation of the urinary bladder epithelium was observed only at dosages in excess of 10 mg/ml.

The 10 mg/ml dosage in drinking water that was applied in the above 13-week study equates to approximately 750 mg/kg/day received dose. Based on the results of that study, the upper dosage in the present study, 1000 mg/kg/day, is expected to cause some toxicity in the F₀ animals, in terms of effects on body weight, liver and kidney weight, and more particularly in males possibly the exacerbation of chronic progressive nephropathy. The 400 mg/kg/day dosage might cause some lesser/marginal toxicity, while the lower dosages are expected to be without discernible toxicity.

5. TEST AND CONTROL ARTICLES

5.1. TEST ARTICLE: TERTIARY BUTANOL (TBA)

5.1.1. Test Article Category

Chemical intermediate.

5.1.2. Supplier

The Sponsor.

5.1.3. Description

Waxy solid at room temperature, liquid at >77°F (per MSDS).

5.1.4. Physicochemical characteristics and composition

Information on the identity, purity, composition, batch/lot number and any other characteristics that define the test article is on file with the Sponsor, who will supply a Certificate of Analysis pertinent to each batch/lot used in the study for inclusion in the raw data and the final report. Handling procedures and other pertinent information have been provided by the Sponsor in a Material Safety Data Sheet (MSDS).

5.1.5. Storage conditions

Raw and formulated test article will be stored at room temperature.

5.1.6. Stability

The Sponsor will supply Certificate(s) of Stability for inclusion in the raw data and the final report.

5.2. ARCHIVAL SAMPLES

The Testing Facility will retain a sample of each batch/lot of test article used during the course of the study. Such test article samples will be stored at the Testing Facility under the stated storage conditions for the article, for a period of 1 year following issue of the final study report (or until the stated expiry date of the samples is reached, whichever is sooner). The samples may then be discarded, or other arrangements made as for other archival materials, by agreement with the Sponsor.

5.3. UNUSED TEST ARTICLE

The unused portion of test article, as well as any empty test article containers, will be returned to the Sponsor following completion of the study.

5.4. CONTROL ARTICLE (DOSING VEHICLE)

The dosing vehicle will be distilled, de-ionized water.

5.5. PREPARATION OF DOSING FORMULATIONS

The formulations will be prepared weekly. The bulk container will be warmed sufficiently to render the contents liquid and the requisite quantity of test article will be weighed into a suitable warmed graduated container. Warmed vehicle will be added and the article mixed by agitation/inversion of the container until a clear solution has formed. The formulation will then be brought up to the required volume and thoroughly re-mixed.

Each formulation will be divided into the appropriate number of daily aliquots on the day of preparation and stored at room temperature. The containers will have the minimum of headspace and will be securely closed.

5.6. UNUSED DOSING FORMULATION

Any unused dosing formulation will be discarded daily, with due precaution, after completion of animal dosing.

5.7. ANALYSIS OF DOSING FORMULATIONS

Formulation concentration and stability analyses will be performed by the Huntingdon Life Sciences Analytical Chemistry Laboratory. As the formulations will comprise true aqueous solutions, homogeneity analysis will not be necessary.

Trial formulations will be prepared 8 days prior to the start of treatment, allowed to stand in sealed containers for 4 hours at room temperature, re-mixed by inversion and then sampled in duplicate (2 x 1 ml samples from each). One set of these 1 ml samples will be analysed for concentration using a method previously validated for the purpose, the results being intended to demonstrate 4-hour

stability in support of daily formulation preparation. The duplicate set will be retained frozen at -70°C or below as contingency, pending satisfactory outcome of these first analyses. The trial formulations will then be stored at room temperature for 8 days, after which they will be remixed by inversion and again sampled in duplicate. This second batch of samples will be analysed in parallel with samples taken from formulations used on the first day of dosing in the study, the results being intended to support weekly formulation preparation.

Dosing formulation samples (2 x 1 ml samples from each) will be taken at the beginning and near the end of the dosing period, and on a convenient occasion around the time of littering (total of 3 occasions). One set of 1 ml samples will be analysed initially, the duplicate set being retained as contingency, frozen at -70°C or below.

Any residual samples, and any reserved duplicate samples, will be discarded following acceptance of the final analytical report.

6. TEST ANIMALS

6.1. SPECIES AND STRAIN

Sprague-Dawley albino rats (outbred)

CrI: CD (SD) IGS BR

6.2. SUPPLIER

Charles River Laboratories, Kingston, New York

6.3. ANIMAL REQUIREMENTS/SPECIFICATIONS

6.3.1. Numbers Purchased

<u>Males</u>	<u>Females</u>	<u>Total</u>
63	63	126

6.3.2. Age and Weight

Male rats will be approximately 6 weeks of age at receipt and approximately 8 weeks (200-300 grams) at initiation of treatment.

Female rats will be approximately 6 weeks at receipt and approximately 8 weeks (150-250 grams) at initiation of treatment, nulliparous and non-pregnant.

Animals outside these weight ranges will be used at the discretion of the Study Director.

6.4. ANIMAL HUSBANDRY

6.4.1. Facilities Management/Animal Husbandry

Currently acceptable practices of good animal husbandry will be followed, e.g., Guide for the Care and Use of Laboratory Animals; National Academy Press 1996. Huntingdon Life Sciences is fully accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC).

6.4.2. Veterinary Care

Animals are monitored by the technical staff for any conditions requiring possible veterinary care. If any such conditions are identified, a staff veterinarian will be notified for an examination and evaluation. Animals will be treated as outlined in the Animal Welfare Act Compliance section of this protocol (Section 14.3).

6.4.3. Housing

All animals will be housed individually in stainless steel suspended cages with wire mesh floors and fronts except for the mating period when one male and one female rat will be housed together. During cohabitation (when female rats will be brought to the male rat's cages), male and female rats will then be housed in stainless steel cages of appropriate size for group housing animals. Each cage will be fitted to secure a glass feeder jar with a stainless steel lid. From Gestation Day (GD) 18 and during lactation, the dam will be housed with the litter in plastic "shoebox" cages with bedding. Clean feed jars and fresh feed will be provided at least weekly for periods when feed consumption is not being recorded and at each interval when feed consumption will be recorded.

6.4.4. Feed and Feed Analysis

Certified Rodent Diet, No. 5002 (Meal) supplied by PMI Nutrition International (St. Louis, MO) and provided *ad libitum*.

Analytical certification of batches of feed will be maintained on file by the manufacturer. There are no known contaminants in the feed that are expected to interfere with the objectives of this study.

6.4.5. Water and Water Analysis

Facility water is supplied by Elizabethtown Water Company (Westfield, NJ) and will be provided *ad libitum* to individual animal cages through an automatic watering system.

Water analyses are conducted by Elizabethtown Water Company to assure that water meets standards specified under the EPA Federal Safe Drinking

Water Act Regulations (40 CFR Part 141). Water analysis, provided by the supplier, will be maintained on file at the Testing Facility. In addition, chemical and microbiological analyses are conducted biannually on water samples collected from representative rooms in this facility. Results are maintained on file. There are no known contaminants that are expected to interfere with the objectives of this study.

6.4.6. Bedding Material

Ground corncob bedding (Bed-O'-Cobs® 1/4 inch Irradiated, The Andersons, Maumee, Ohio) will be provided for each mated female rat on GD 18. Fresh bedding will be provided weekly or as needed throughout lactation. There are no known contaminants in the bedding that are expected to interfere with the results of this study.

6.4.7. Environmental Conditions

Light/Dark Cycle

Twelve hour light/dark cycle provided via automatic timer.

Temperature

Temperature will be monitored in accordance with Testing Facility SOPs to ensure that the desired range of 18 to 26°C is maintained to the maximum extent possible.

Humidity

Humidity will be monitored in accordance with Testing Facility SOPs to ensure that the desired range of 30 to 70% is maintained to the maximum extent possible.

6.5. ACCLIMATION PERIOD

This will be for 1-2 weeks. All animals will be checked for viability twice daily. Prior to assignment to the study, all animals will be examined to ascertain suitability for study.

6.6. ANIMAL ASSIGNMENT

More animals than required for the study will be purchased and acclimated. Animals considered suitable for study on the basis of body weight data and any other pre-test evaluations, will be randomly assigned to control or treated groups in an attempt to equalize mean group body weights to within the range $\pm 20\%$ of the mean weight for each sex. Disposition of all animals not utilized in the study will be maintained in the study file.

6.7. ANIMAL IDENTIFICATION

Each animal will be assigned a temporary identification number upon receipt. After selection for study, each animal will be ear-tagged with a number assigned by the Testing Facility. This number plus the study number will comprise the unique animal number for each animal. If the tag is lost, it will be replaced or the animal will be tattooed for identification. Each cage will be provided with a cage card that will be color-coded for dose level identification and will contain the study number and animal number.

6.8. MATING PROCEDURE

Within each treatment group the animals will be paired, 1 male to 1 female in the male's cage, until evidence of mating is seen or for 2 consecutive weeks. The females will be observed early each morning for the presence of a vaginal plug or sperm in the vaginal smear. The day on which positive evidence of mating is observed will be defined as gestation day (GD) 0. Once mated, the female will be removed from the mating cage and housed individually for the remainder of the study. After the mating period is over, female rats without evidence of copulation will also be removed, housed individually and monitored for visible signs of pregnancy.

7. TEST ARTICLE ADMINISTRATION

7.1. ROUTE OF ADMINISTRATION

Oral, by gavage.

7.2. FREQUENCY AND DURATION OF ADMINISTRATION

Males will be dosed once daily, seven days/week for 4 weeks prior to mating initiation, continuing through the mating and post-mating periods until termination after a minimum of 9 weeks of treatment. Females will be dosed once daily, seven days/week, for 4 weeks prior to mating initiation, continuing through mating, gestation and lactation until post-natal day (PND) 20. Females that do not produce a litter will continue to be treated for up to 24 days following completion of the mating period, and will be terminated on the 25th day after the last exposure to a male.

7.3. ADMINISTRATION OF TEST ARTICLE

The dosing formulations will be administered by gavage; a suitably sized flexible catheter attached to an appropriately sized syringe. Dosing formulations will be re-mixed by inversion prior to opening for dosing. Dosage volume (5 ml/kg body weight) will be calculated for each animal using the most recent body weight recorded, excepting for F₀ females the period of gestation after GD 17, during which the dose volume will remain fixed according to the GD 17 body weight

until the animal has completed parturition. If at the time of dosing an animal has commenced, but not completed parturition, it will not be dosed on that day. Following completion of parturition, dosage volume for each female will revert to being determined by the most recent body weight recorded.

8. IN-LIFE EXPERIMENTAL OBSERVATIONS

8.1. CLINICAL OBSERVATIONS

8.1.1. Viability Observations (Cageside)

Observations for mortality, morbidity, or signs of severe toxicity will be made at least twice daily, prior to dosing during the treatment period, then again late in the work day. Animals in apparently poor health or a moribund condition will be identified for further monitoring and possible euthanasia.

8.1.2. Post-Dose Observations (Cage side and/or in the hand)

Each animal will be checked for overt signs of toxicity prior to dosing and any changes from the preceding observation will be recorded. Each dosed animal will then be observed approximately one to two hours after dosing. Further observations may be made at intervals subsequently, as found appropriate.

8.1.3. Detailed Physical Observations

The animals will be examined cage-side and in the hand prior to randomisation into the treatment groups, then once weekly through to terminal euthanasia, for any abnormality or sign of toxicity. Examinations will include observations of general condition, skin and fur, eyes, nose, oral cavity, abdomen and external genitalia, occurrence of secretions and excretions, autonomic activity (*eg* lacrimation, piloerection, pupil size, unusual respiratory pattern). Changes in gait, posture and response to handling, the presence of clonic or tonic movements, stereotypy (*eg* excessive grooming, repetitive circling) or bizarre behaviour (*eg* self-mutilation, walking backward) will be recorded. During the treatment period this evaluation will be performed prior to dosing, and for mated females it will coincide with GD 0, 7, 14, 20 and PND 1, 7, 14 and 21.

8.2. BODY WEIGHTS

Body weights of the F₀ animals will be recorded at the time of randomization into test groups, on the day treatment is initiated and weekly thereafter until pairing for mating. Males will continue to be weighed weekly until termination, but for mated females weights will be taken on GD 0, 7, 14 and 20, and for those that

deliver litters, on PND 1, 4, 7, 14 and 21. Females without evidence of mating will continue to be weighed weekly until termination, unless they deliver a litter.

Directly dosed F_1 offspring will be weighed on PND 21, 24 and 28.

A terminal body weight (non-fasted) will also be recorded for each F_0 and F_1 (post-weaning) animal.

Pre-weaning F_1 pups will be weighed individually on PND 1, 4, 7, 14 and 21.

8.3. FEED CONSUMPTION

Feed consumption for the F_0 animals will be recorded weekly during the 4-week pre-mating treatment period, but not during the mating period when females are cohabited with males. For mated females, feed consumption will be recorded on GD 0-7, 7-14 and 14-20, and on PND 1-4, 4-7 and 7-14. Weekly measurements will resume for males after completion of the mating period, and also for any females without a sign of mating, until termination.

Feed consumption will be measured for the cages of directly dosed F_1 offspring on PND 21-24 and 24-28.

8.4. PARTURITION AND LACTATION

On GD 18, several days prior to expected parturition, mated females will be transferred to solid, plastic cages with bedding material.

8.4.1. Observations

After GD 18, examination for signs of parturition will be made twice daily (morning and afternoon). Evidence of difficult or prolonged parturition, if observed, will be recorded. The day on which parturition is initiated will be defined as PND (lactation day) 0. The duration of gestation will be deduced. Litters will be observed as soon as possible after parturition for the number of live and dead pups, any pup abnormalities and the sex of each pup. All pups in the litter will be uniquely identified by toe tattoo after parturition is complete. Thereafter, litters will be observed twice daily (morning and afternoon). The presence of dead pups will be recorded and these will be removed from the cage as found. Unusual observations, signs of deficient maternal care and pups without milk in the stomach will be recorded.

8.4.2. Culling

On PND 4, each litter of more than ten pups will be randomly culled to that number with sex distribution equalized (up to five/sex) where possible.

8.5. F₁ PUP EVALUATIONS

8.5.1. Pup Physical Examinations

Each pup will be given a gross physical examination and sexed on PND 0 (if parturition is complete), 1, 4 (pre-cull), 7, 14 and 21. The pups will also be observed for any abnormal behaviour.

8.5.2. Body Weight

Individual pup body weights will be recorded on PND 1, 4 (pre-cull), 7, 14 and 21.

8.6. SELECTION OF F₁ ANIMALS

Nominally, 1 male and 1 female offspring will be randomly selected at weaning (PND 21) from each available litter, for subsequent direct treatment. Grossly abnormal animals within the litters will be excluded from selection, if in the judgment of the Study Director their condition may adversely affect survival. Runts, if otherwise normal, will not be excluded from the selection procedure.

This will be to constitute a nominal group size of 12 offspring of each sex per group. If, after the initial selections, the group size is less than 10 for any sex, that number will be made up to 10 by selection of further pups.

The selected weanlings will be individually identified by means of metal ear-tags and housed two or three per cage, by sex, until termination on PND 28.

The dams and the unselected weanlings will be euthanized on PND 21.

9. TERMINATION

9.1. TERMINATION SCHEDULE

9.1.1. F₀ Males

F₀ males will be sacrificed after at least 9 weeks of treatment.

9.1.2. F₀ Females

F₀ females with litters will be sacrificed on PND 21. Females that mated but failed to deliver a litter will be sacrificed at least 25 days after evidence of mating. Females for which no evidence of mating was detected and which failed to deliver a litter will be sacrificed at least 25 days after their last exposure to a male. Females that show total litter loss before weaning will be retained on treatment until it is clear that further mating in the study will not be necessary, and then sacrificed as convenient.

9.1.3. F₁ Offspring, post-weaning

The offspring selected for direct treatment will be sacrificed on PND 28.

9.1.4. F₁ Offspring, non-selected

Those offspring not selected for direct treatment will be sacrificed on PND 21.

9.2. METHODS OF EUTHANASIA

All post-weaning animals will be euthanized by exposure to carbon dioxide. Pre-weanlings will be euthanized by intraperitoneal injection of sodium pentobarbitone.

10. TERMINAL OBSERVATIONS**10.1. F₀ ANIMALS****10.1.1. Necropsy**

A macroscopic necropsy will be performed on all F₀ animals, including those dying spontaneously or euthanized in a moribund condition, and any females sacrificed following litter loss. This will include examination of external surfaces, all orifices, cranial cavity, neck and its associated tissues and organs, thoracic, abdominal and pelvic cavities and their associated tissues and organs, and external surfaces of the brain. The number of implantation sites will be recorded for each F₀ female rat. Apparently non-pregnant status will be confirmed by Salewski staining. Gross lesions or tissues with significant findings may be preserved in 10% neutral buffered formalin (NBF) at the discretion of the necropsy supervisor or the Study Director, to determine the pathological condition.

10.1.2. Organ Weights

For all F₀ animals, excepting any found dead, the organs indicated below will be removed at necropsy, carefully trimmed to remove fat and other contiguous tissue and will be weighed as soon as possible after dissection to avoid drying. Paired organs will be weighed separately.

Males	Females
Testes	Liver
Epididymides	Kidneys
Kidneys	
Liver	

10.1.3. Seminology

For F₀ males at scheduled necropsy, the following sperm evaluations will be performed by Pathology Associates International (PAI), Frederick, Maryland:

The right vas deferens will be excised and placed in a pre-warmed solution of phosphate buffered saline and 1% Bovine Serum Albumin. After a minimum 3-minute "swim-out" period, a sample will be placed in a Hamilton Thorne IVOS sperm analyzer and five microscope field images will be stored electronically. For the Control and High dose groups initially, these fields will be analyzed for percent motility.

The right testis and epididymis will be frozen on dry ice for transport to PAI, Frederick, MD. These organs will be stored frozen at -70°C or below until evaluation for sperm count (spermatids in the testis). Initially for the Control and High dose groups only, the epididymis will be thawed and the caudal portion removed and weighed. Homogenized samples of the caudal epididymis and the testis will be stained and examined using a Hamilton Thorne IVOS sperm analyzer. For each stained preparation, 20 fields will be counted. The total number of sperm in the caudal epididymis, or spermatids in the testis, will be calculated and reported adjusted for organ weight. Additionally, two sperm morphology slides will be prepared for each male, stained with Eosin and then evaluated for morphological development (at least 200 cells evaluated for each animal).

Option: If findings in these analyses warrant further investigation, by agreement with the Sponsor, the samples/motility fields from the Mid and Low dose groups may also be analyzed, at additional cost.

10.1.4. Tissues Preserved

Tissues listed in the following table will be obtained at necropsy for all F₀ animals in each group and preserved in 10% neutral buffered formalin (NBF), with the exception of testes, which will be preserved in a modified Davidson's fixative for 48-72 hours and then stored in NBF.

Tissue	Tissues Preserved	Microscopic Examination
Testis (1)	X	X
Epididymis (1)	X	X
Seminal vesicles (2) with coagulating gland	X	Optional

Tissue	Tissues Preserved	Microscopic Examination
Prostate	X	Optional
Ovary (2) with oviducts	X	X
Thyroids with parathyroids	X	X
Kidneys (2)	X	Optional
All Macroscopic lesions/abnormalities	X	Optional

10.1.5. Histopathology

Microscopic examinations for Control and High dose group F₀ animals will be performed on the tissues and organs designated in the preceding table. During the microscopic examination of the testes, special attention will be paid to the stages of spermatogenesis and interstitial testicular cell structure. If treatment-related changes are observed in the High dose group, microscopic examinations will be extended to the Mid and Low dose groups (*additional cost*).

Stains: Standard stains (haematoxylin and eosin) will be used. Special stains may be employed on selected tissues to aid in making a diagnosis, at the discretion of the Study Pathologist.

10.2. F₁ OFFSPRING: NON-SELECTED WEANLINGS (PND 21), AND DIRECTLY TREATED (PND 28)

A necropsy will be performed on all these animals, including any of the directly treated animals (only) that die spontaneously or are euthanized in a moribund condition during their treatment period. This will include macroscopic examination of external surfaces, all orifices, cranial cavity, neck and its associated tissues and organs, thoracic, abdominal and pelvic cavities and their associated tissues and organs, and external surfaces of the brain. Gross lesions or tissues with significant findings may be preserved in 10% neutral buffered formalin at the discretion of the necropsy supervisor or the Study Director, to determine the pathological condition.

10.3. F₁ PUPS: CULLED ON PND 4

A macroscopic external examination will be performed for all F₁ pups culled on PND 4. Externally normal pups will be discarded without necropsy. Pups with any apparent abnormality will be preserved for optional further examination. Absence of milk in the stomach (presence/absence visible externally, through the skin) will be noted.

10.4. F₁ PUPS: DECEDENT PRIOR TO WEANING

A macroscopic external examination will be performed for all F₁ pups found dead or sacrificed moribund prior to weaning. A necropsy will be performed where practicable, including examination of the thoracic, abdominal and cranial contents for any grossly apparent abnormalities, but no tissues will be preserved. Where possible, the presence or absence of milk in the stomach will be determined.

11. PRESERVATION OF RECORDS AND SPECIMENS

All data documenting experimental details and study procedures and observations will be recorded and maintained as raw data. At the completion of the study, all reports, raw data, preserved archival specimens and retained samples will be maintained in the Testing Facility's Archives for a period of 1 year after submission of the signed final report.

The Sponsor will be contacted in order to determine the final disposition of these materials. The Sponsor is responsible for all cost associated with the storage of these materials beyond 1 year from the issuance of the final report and for any costs associated with the shipment of these materials to the Sponsor or to any other facility designated by the Sponsor.

12. STATISTICAL EVALUATIONS**12.1. CONTINUOUS DATA**

Including, but not limited to:

Body weights

Body weight changes

Feed consumption values

Mean number of uterine implantations

F₁ pup weights, by sex and composite (each weighing interval during lactation)

Litter size

Organ weights and organ weight to body weight ratios

Evaluation of equality of group means will be made by an appropriate statistical method, followed by a multiple comparison test if needed. Bartlett's test (Bartlett, 1937; Sokal and Rohlf, 1995) will be performed to determine if groups have equal variances. For all parameters except organ weights, if the variances are equal, parametric procedures will be used; if not, nonparametric procedures will be used.

Organ weight data will be analyzed only by parametric methods. The parametric method will be the standard one-way analysis of variance (ANOVA) using the F ratio to assess significance (Armitage, 1971; Dunlap and Duffy, 1975). If significant differences among the means are indicated, additional tests will be used to determine which means are significantly different from the control: Dunnett's (Dunlap et al., 1981; Dunnett, 1955, 1964), Williams (Williams, 1971, 1972), or Cochran and Cox's modified t-test (Cochran and Cox, 1959). The nonparametric method will be the Kruskal-Wallis test (Kruskal and Wallis, 1952, 1953) and if differences are indicated, Shirley's test (Shirley, 1977), Steel's test (Steel, 1959), or Pairwise Comparison with Bonferroni Correction (Games and Howell, 1976) will be used to determine which means differ from control. Bartlett's test for equality of variance will be conducted at the 1% significance level; all other statistical tests will be conducted at the 5% and 1% significance levels.

References for these procedures are:

Armitage, P. 1971. Statistical Methods in Medical Research. Oxford, UK: Blackwell Scientific Publications

Bartlett, M.S. 1937. Properties of sufficiency and statistical tests. Proceedings of the Royal Society, Series A, 160: 268-282

Cochran, W.G. and Cox, G.M. 1959. Experimental Designs, New York: John Wiley, pp. 100-102

Dunlap, W.P. and Duffy, J.A. 1975. Fortran IV Functions for Calculating Exact Probabilities Associated with Z, Chi-Square, T and F Values. Behav. Res. Methods and Instrumentations 7:59-60

Dunlap, W.P., Marx, M.S. and Agamy, G.G. 1981. Fortran IV functions for calculating probabilities associated with Dunnett's test. Behav. Res. Methods and Instrumentation 13: 363-366

Dunnett, C.W. 1955. A multiple comparison procedure for comparing several treatments with a control. Journal of the American Statistical Association 50: 1096-1121

Dunnett, C.W. 1964. New tables for multiple comparisons with a control. Biometrics 20-3: 482-491

Games, P.A. and Howell, J.F. 1976. Pairwise multiple comparison procedures with unequal n's and/or variances: a monte-carlo study. Journal of Educational Statistics 1: 113-125

Kruskal, W.H. and Wallis, W.A. 1952. Use of Ranks in one-criterion variance analysis. *Journal of the American Statistical Association* 47: 583-621

Kruskal, W.H. and Wallis, W.A. 1953. Errata for Kruskal-Wallis (1952) *Journal of the American Statistical Association* 48: 907-911

Shirley, E.A.C. 1977. A non-parametric equivalent of Williams' test for contrasting increasing dose levels of a treatment. *Biometrics* 33: 386-389

Sokal, R.R. and Rohlf, F.J. 1995. *Biometry*. 3rd Edition. San Francisco: W.H. Freeman pp. 369-371

Steel, R.G.D. 1959. A multiple comparison rank sum test: treatment versus control. *Biometrics* 15: 560-572

Williams, D.A. 1971. A test for differences between treatment means when several dose levels are compared with a zero dose control. *Biometrics* 27: 103-117

Williams, D.A. 1972. The comparison of several dose levels with a zero dose control. *Biometrics* 28: 519-531.

12.2. INCIDENCE DATA

Including, but not limited to:

Mortality incidence

Mating indices, pregnancy rates, fertility indices

Gestation indices

Incidence of dams with no viable pups

Incidence of pathological abnormalities

A Fisher Exact Test with Bonferroni correction will be performed to identify differences between the control and treatment groups. All statistical tests will be conducted at the 5% and 1%, two-sided significance levels.

13. REPORTING

13.1. STATUS REPORTS

The Contractor will provide progress reports to the Sponsor at appropriate intervals.

13.2. FINAL REPORT

The Testing Facility will provide the Sponsor with one copy (additional copies will be at additional cost) of a draft of the final report. The final report will include but not be limited to the following:

13.2.1. Body of Report

- GLP Compliance Statement
- Quality Assurance Statement
- Summary
- Introduction
- Experimental Design
- Materials and Methods
- Results and Discussion
- Conclusions
- Statistical Procedures
- Protocol deviations and study impact statements

13.2.2. Summary Tables

- Dosing formulation analysis
- Mortality
- Mating indices, pregnancy rates and male rat fertility indices
- Physical in-life observations
- Mean body weight data - Male and female pre-mating; females during gestation and lactation; males after mating
- Mean animal weight gain data - Pre- and post-mating; female rats during gestation and lactation
- Mean feed consumption data - Male and female pre-mating; females during gestation and lactation; males after mating
- Mean gestation length
- Mean number of uterine implantation sites
- Mean female rat litter data to include the number of pups (live, dead and total) at birth and number of live pups through lactation
- Litter survival indices
- Mean litter pup survival indices
- Mean pup weights
- Mean pup sex ratio
- Macroscopic postmortem examinations
- Mean organ weights and organ/body ratios
- Microscopic Pathology

13.2.3. Appendix Tables (Individual data)

- Mortality
- Mating indices, pregnancy rates and male rat fertility indices
- Physical in-life observations
- Mean and individual body weight data - Male and female pre-mating; females during gestation and lactation; males after mating
- Mean and individual animal weight gain data – Pre- and post-mating; females during gestation and lactation
- Individual feed consumption data - Male and female pre-mating; females during gestation and lactation; males after mating
- Individual gestation length
- Individual number of uterine implantation sites
- Individual female rat litter data to include the number of pups (live, dead and total) at birth and number of live pups through lactation
- Individual litter survival indices
- Individual litter pup survival indices
- Individual pup weights
- Individual macroscopic postmortem examinations
- Individual organ weights and organ/body ratios
- Individual Microscopic Pathology

13.2.4. Miscellaneous Appendices

- Personnel involved in the study
- Protocol and Amendments

14. REGULATORY REFERENCES**14.1. TEST GUIDELINE**

This study complies with or exceeds the Organization for Economic Cooperation and Development (July 27, 1995) OECD Guidelines for Testing of Chemicals, OECD Guideline 421: Reproduction/Developmental Toxicity Screening Test.

14.2. GOOD LABORATORY PRACTICES

This study will be conducted in compliance with EPA Good Laboratory Practices as set forth in 40 CFR Part 792 (TSCA) and Organization for Economic Cooperation and Development (OECD) Good Laboratory Practices as set forth in ENV/MC/CHEM(98)17.

14.3. ANIMAL WELFARE ACT COMPLIANCE

This study will comply with all appropriate parts of the Animal Welfare Act regulations: 9 CFR Parts 1 and 2 Final Rules, Federal Register, Volume 54, No. 168, August 31, 1989, pp. 36112-36163 effective October 30, 1989 and 9 CFR Part 3 Animal Welfare Standards; Final Rule, Federal Register, Volume 56, No. 32, February 15, 1991, pp. 6426-6505 effective March 18, 1991. The Sponsor should make particular note of the following:

The Sponsor's signature on this protocol documents for the study described, that there are no generally accepted non-animal alternatives and the study does not unnecessarily duplicate previous experiments.

All procedures used in this study have been designed to avoid discomfort, distress and pain to the animals. All methods are described in this study protocol or in written laboratory standard operating procedures.

Any procedures outlined in this study protocol which are expected to cause more than momentary or slight pain or distress to the animals will be performed with appropriate sedatives, analgesics or anesthetics unless the withholding of these agents is justified for scientific reasons, in writing, by the Sponsor and the Study Director and approved by the IACUC; in which case the procedure will continue for the minimum time necessary. Documentation of the justification for withholding treatment for pain or distress and IACUC approval of the procedures will be made prior to study initiation on the IACUC Protocol Review form.

Animals experiencing more than momentary or slight pain or distress due to test article or emergency situations, such as injury or illness, will be treated by the Testing Facility's veterinarian staff with approved analgesics or agents to relieve pain. If possible, the Study Director will be consulted prior to treatment; however, the veterinary staff is authorized to administer emergency treatment as necessary. Any subsequent treatment or euthanasia will be administered after consultation with the Study Director. The Sponsor will be advised by the Study Director of all emergency situations in as timely a manner as possible.

Methods of euthanasia used in this study are in conformance with the above referenced regulations.

**14.4. INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE
(IACUC)**

The IACUC Protocol Review Subcommittee has reviewed this protocol and found it to be in compliance with appropriate animal welfare regulations.

15. QUALITY ASSURANCE MONITORING

The Quality Assurance Unit of Huntingdon Life Sciences (East Millstone, NJ) will monitor the facilities, equipment, personnel, methods, practices, records, raw data, draft and final reports and controls used in this study to assure that they are in conformance with this protocol, company Standard Operating Procedures and the referenced Good Laboratory Practice regulations.

16. ALTERATION OF DESIGN

Alterations of this protocol may be made as the study progresses. No changes in the protocol will be made without the consent of the Sponsor. In the event that the Sponsor authorizes a protocol change verbally, such changes will be honored by the Testing Facility and will be followed by a written verification. All protocol modifications will be signed by the Study Director and a Sponsor representative. Any modifications potentially affecting animal welfare will also be signed by two members of the Institutional Animal Care and Use Committee prior to the modification's implementation.

Protocol Amendment No. 1

Study Title: **TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY
SCREENING STUDY IN RATS**

Protocol Issue No.: Final

Changes (old text scored through, new text underlined)

1. Page 14: SECTION 8.2 BODY WEIGHTS

Mated female body weights will also be recorded on GD 17.

2. Page 19: SECTION 10.3 F₁ PUPS: CULLED ON PND 4

Third sentence: Pups with any apparent abnormality (other than superficial damage such as bruising) will be preserved for optional further examination.

3. Page 20: SECTION 10.4 F₁ PUPS: DECEDENT PRIOR TO WEANING

First sentence: A macroscopic external examination will be performed for all F₁ pups found dead or sacrificed ~~meribund~~ prior to weaning.

Reasons for Changes

1. To correct the omission of a particular body weight that will be required to be recorded for the dams.
 2. To eliminate the need for preservation of culled pups with common incidental findings at termination.
 3. To ensure that the provisions of this section apply to those otherwise normal pups that are killed as a consequence of demise of the dam prior to weaning.
-

No additional costs are associated with this amendment.

Protocol Amendment No. 2

Study Title: **TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY
SCREENING STUDY IN RATS**

Protocol Issue No.: Final

Changes (where appropriate, old text shown scored through, new text underlined)

1. Page 5: SECTION 3. PROPOSED STUDY DATES

Add: Experimental Start Date: 12 June 2003
Experimental Completion Date: 24 November 2003
(Estimated date of completion of
histopathology report)

**2. Page 13: SECTION 7.2 FREQUENCY AND DURATION OF
ADMINISTRATION**

~~Males-F₀ males~~ will be dosed once daily, seven days/week for 4 weeks prior to mating initiation, continuing through the mating and post-mating periods until termination after a minimum of 9 weeks of treatment. ~~Females-F₀ females~~ will be dosed once daily, seven days/week, for 4 weeks prior to mating initiation, continuing through mating, gestation and lactation until post-natal day (PND) 20. Females that do not produce a litter will continue to be treated for up to 24 days following completion of the mating period, and will be terminated on the 25th day after the last exposure to a male.

Selected F₁ offspring, following weaning, will be dosed once daily on PND 21-27,
with termination on PND 28.

Reasons for Changes

1. To insert experimental start and completion dates (collection of first data and completion of data collection).
 2. To correct the omission of mention in protocol Section 7.2 of direct dosing of selected F₁ offspring after weaning.
-

Huntingdon Life Sciences


03-4254

Page 2 of 2

Protocol Amendment No. 2


No additional costs are associated with this amendment.

Amendment approved by:




Keith P Hazelden, BSc, CBiol, MIBiol
Study Director
Huntingdon Life Sciences

1 Aug 03
Date



Sylvie J Gosselin, DVM, PhD, ACVP
Facility Management
Huntingdon Life Sciences

28 Aug 03
Date



George Cruzan, PhD, DABT
Study Monitor
ToxWorks

August 13, 2003
Date

Protocol Amendment No. 3

Study Title: **TBA: REPRODUCTION/DEVELOPMENTAL TOXICITY
SCREENING STUDY IN RATS**

Protocol Issue No.: Final

Changes (where appropriate, old text shown scored through, new text underlined)

1. Page 13: SECTION 7.3. ADMINISTRATION OF TEST ARTICLE

The dosing formulations will be administered by gavage; a suitably sized flexible catheter attached to an appropriately sized syringe. Dosing formulations will be re-mixed by inversion prior to opening for dosing. Dosage volume (5 ml/kg body weight) will be calculated for each animal using the most recent body weight recorded, excepting for F₀ females the period of gestation after GD 17, during which the dose volume will remain fixed according to the GD 17 body weight until the animal has completed parturition. If at the time of dosing an animal has commenced, but ~~does not completed~~ complete parturition by approximately 1400 hours, it will not be dosed on that day. ~~Following completion of~~ For females that have completed parturition, dosage volume ~~for each female~~ will revert to being determined by the most recent body weight recorded, commencing with the weight recorded on PND 0 or PND 1, as appropriate (see Section 8.2, as adjusted in this Amendment, below).

2. Page 14: SECTION 8.2 BODY WEIGHTS

First paragraph:

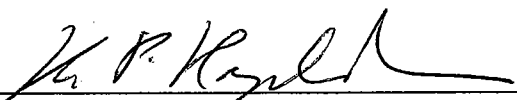
Body weights of the F₀ animals will be recorded at the time of randomization into test groups, on the day treatment is initiated and weekly thereafter until pairing for mating. Males will continue to be weighed weekly until termination, but for mated females weights will be taken on GD 0, 7, 14 and 20, and for those that deliver litters, on PND 1, 4, 7, 14 and 21. F₀ female body weight will also be recorded on PND 0, if the animal has completed parturition. If the animal has not completed parturition and consequently is not dosed on that day, no PND 0 weight will be recorded for that animal. Females without evidence of mating will continue to be weighed weekly until termination, unless they deliver a litter.

Protocol Amendment No. 3**Reasons for Changes**

1. To clarify the requirements for dosing of females on the day of parturition.
 2. To include a body weight on PND 0, so that dosage volume administered on that day to animals that have completed parturition is based on a relevant post-parturition body weight, and not on a weight taken in mid-late pregnancy.
-


No additional costs are associated with this amendment.

Amendment approved by:



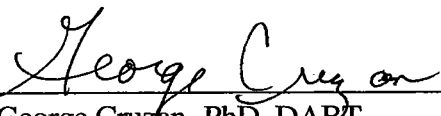
Keith P Hazelden, BSc, CBiol, MIBiol
Study Director
Huntingdon Life Sciences

7 Aug 03
Date



Sylvie J Gosselin, DVM, PhD, ACVP
Facility Management
Huntingdon Life Sciences

28 Aug 03
Date




George Cruzan, PhD, DABT
Study Monitor
ToxWorks

Aug. 13, 2003
Date

Protocol Amendment No. 1


Amendment approved by:



Keith P Hazelden, BSc, CBiol, MIBiol
Study Director
Huntingdon Life Sciences

16 Jun 03

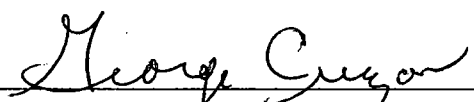
Date



Sylvie J Gosselin, DVM, PhD, ACVP
Facility Management
Huntingdon Life Sciences

16 June 03

Date



George Cruzan, PhD, DABT
Study Monitor
ToxWorks

June 17, 2003

Date

	Report Amendments	Appendix II
--	-------------------	-------------

There are no amendments for this report at this time.